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* Annual address delivered at the Central London Throat, Nose and Ear Hospital on Oct. 12th, 1934.



### Diagnosis

It will now be obvious that it is most important to try to arrive at a correct diagnosis before deciding upon the treatment. It is indeed regrettable that in their early stages these growths should give rise to so little discomfort. Usually there is no obvious swelling as in other parts of the body, pain is rarely an early symptom, and bleeding generally insignificant. The symptoms are those of slight general inflammation. There may be a thin indefinite discharge—sometimes blood-stained or offensive. When these occur in an elderly patient who has never had previous trouble in his antrum the possibility of cancer must be considered, but until we have an exact test for cancer a larger proportion of these cases than is generally realised will be overlooked. Usually transillumination shows a dense shadow on the affected side but X rays are often of little value because visible bone changes occur late. Injections of lipiodol however before radiography may reveal filling effects and be helpful. Negative antral puncture is of little value but if blood-stained serum is found the antrum should be explored to confirm the diagnosis.

*Biopsy.*—It seems generally agreed that many of these growths can be easily disseminated through the vessels and lymphatics to the deeper parts. Therefore when making a biopsy all soft tissues should for preference be divided by the endotherm knife and the fragment removed with as little disturbance as possible and from the most accessible region. Recently we have made a rule to give a short course of deep X rays—about one-third dose—before the biopsy is undertaken. Unfortunately negative histological reports are common and cause dangerous delays. Repeated minor operations are invariably disastrous; many of our patients have had numerous intranasal treatments for removal of polypi or external exploratory treatments before they come to our hospitals. Both in this region and in other parts of the body I would like to see a general rule recognised that if a growth is suspected it should never be disturbed, even for a biopsy, until the patient has been admitted to some institution where appropriate treatment can be given. When we can persuade the medical profession that partial operations on cancers amount to malpractice we shall be able to obtain a much higher proportion of good results. In the upper jaw there need be no doubts about the diagnosis, for practically all tumours are malignant growths and, at the risk of being tedious, I should like to emphasise how dangerous it is to disturb them. All of us have repeatedly seen cases such as the patient with the small encapsuled endothelioma which has been removed locally and then extensively but has recurred so as not only to fill up the whole of the cavity in the jaw but has extended to the glands and even to other parts of the body. The carcinomas and sarcomas are even more prone to behave in this manner. Many of our patients have been sent to us for ray treatments after exploratory operations such as Moure's, Rouge's or partial or even complete resection of the jaw, and although the local growths nearly always respond to irradiation and in some cases may entirely disappear the improvement is only temporary as local recurrences or metastases develop in other parts of the body and the patients rarely live for 12 months. Therefore it must be clearly recognised that ray treatment for these growths which have been previously operated upon are given for palliation of symptoms.

## Treatment

The combination of surgery, diathermy, and irradiation marks the great advance that has been made in the treatment of these cases. The main purpose of this report is to emphasise that no surgeon can undertake these cases unless he has all these methods at his disposal. We must no longer balance these three treatments one against the other but employ them all in different combinations according to the nature of the disease. Although the details of our treatment must be constantly modified to suit the case, a fairly regular method can usually be applied. When a growth is suspected a short course of irradiation should be given over three or four days amounting to about one-third of a full course of high-voltage X rays. This often produces distinct shrinking of the neoplasm but rarely of inflammatory conditions.

### OPERABLE CASES

For these types surgery and diathermy are indispensable because up to the present it has not been found possible to deliver an adequate dose to such growths which are so deeply situated by surface treatment alone. It has been found that complete removal of the upper jaw is no longer advisable. Personally I do not believe that the approach should ever be made through the skin. As most of these growths are complicated by sepsis the first essential is to provide free drainage and this can be obtained by an opening below either through the canine fossa or through the palate. For preference all the soft tissues should be divided by an endotherm knife; the canine fossa should be opened first and if the antrum is found to be full of growth the hard palate should be removed (Fig. 1). As a rule the soft palate should be preserved even if it is thought that the growth has invaded it because in this situation

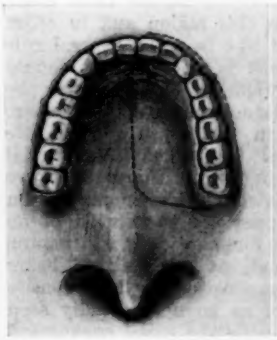

FIG. 1.—Incision for the removal of the hard palate.

FIG. 2.—Removal of tumour by diathermy.

the disease can be successfully treated by irradiation, using surface or interstitial needling. If the soft palate can be left intact and ultimately becomes healthy a very simple denture will repair all the deformity and make the patient comfortable again.

The question of dental sepsis is also very important. In all cases all septic teeth should be removed at this stage. Unless the growth is very localised I prefer to make a large opening, which necessitates taking away the whole of the alveolus with the teeth on the affected side from the middle line in front to the wisdom tooth behind. Otherwise it is impossible to obtain a really free exposure of the growth or to avoid leaving deep recesses which are difficult of access. A large opening gives a good exposure of the antrum, the nasal fossa and the other accessory sinuses, even the ethmoids and sphenoids. If the tumour is massive it is generally advisable to remove the greater part of it through this opening, and if diathermy is employed the risk of dissemination is diminished. In any case it is advisable to get rid of as much ulceration and necrotic tissue as possible, particularly when dealing with low-grade tumours (Fig. 2). If the growth is known to be very cellular it may be safer to treat it by irradiation alone after removal of the palate.

Transpalatal exposure is a simple operation and can be performed rapidly with very little loss of blood and hardly any shock. Intratracheal anæsthesia should be employed and the pharynx plugged securely with gauze so that blood and pus are prevented from passing down into the lungs. Complications such as sepsis and secondary hæmorrhage are rare. There need be no mortality. After four or five days the outlying malignant cells, which are always present in the bony structure surrounding the cavity and which can rarely be destroyed even by heat, should be treated by irradiation. Different methods have been employed in various centres including massive doses for short periods and smaller amounts over a longer time. Personally I prefer radium to X rays, and surface rather than interstitial needling or seeds. Quick however inserts radon seeds and has published good results. After careful consideration of the different methods I have come to the conclusion that the best results can be obtained by slow and prolonged treatments. My experience of cancer in this region goes to show that it can rarely be destroyed quickly however massive a dose is given. The routine that we now employ is as follows:—

*Surface Irradiation.*—About the fifth day after removal of the palate a dental plate is made consisting of two parts. The upper consists of a soft dental material which is moulded to fit the cavity accurately—the lower of vulcanite containing a layer of lead to protect the tongue and the mouth from unnecessary irradiation. Upon the surface of the upper stent radium needles of different lengths are applied containing 0·5 to 1 mg. each; 15 to 20 mg. of radium in all are employed. Filtration should be at least 0·8 mm. of platinum. With smaller filtration, such as 0·5 mm. of platinum, it has been found that the reactions are more intense and cause not only pain and discomfort but may result in serious sloughing and necrosis later on. The needles are covered thinly with soft stent so that the surface of the plate is smooth. It is inserted into the cavity and kept in place by the lower plate (Fig. 3). In practice it has been found that the best results have been obtained by splitting the dose. The plate is worn at first for periods of two hours night and morning with a tendency to increase the time towards the end of the treatment. This process is continued for 10 to 20 days until a total dose of 1000 to 2000 mg. hours has been given, by which time the growth if not removed should have shrunk greatly and the cavity should be covered with a thick yellow film. By using split doses the normal tissues should not be seriously damaged because they have long periods of rest and if the patients use frequent mouth washes they do not become greatly inflamed. The effect upon the disease can be watched from day to day and if necessary the position of the radium can be changed so as to intensify the dose in any particular region. When a growth is localised inside the antrum it is comparatively easy to destroy it completely, but if, as so often happens, the extensions of the disease

are uncertain it may be advisable to employ external irradiation through the skin or through the mouth and particularly to keep in mind the ethmoidal region and orbit. It is these situations that are more likely to receive inadequate treatment and most of our failures have been due to recurrences in them. I find it very difficult to deal with this complication; whenever it appears likely that the disease may have affected the higher cells additional needles or seeds are inserted interstitially through the roof of the cavity, through the nose or through the skin into the inner part of the orbit and ethmoidal region and retained for a week. This method or some slight variation of it is now exclusively employed as I consider that nothing is gained by making a mutilating incision through the skin or by removal of the whole of the jaw. After the growth has been destroyed the palatal opening can be closed by a well-fitting dental plate which allows the patient to speak and feed easily. A point of the greatest importance is that the permanent opening allows the cavity to be inspected easily so that at any time if there is any remnant of disease or recurrence it can be treated by diathermy or by further irradiation. When a successful result is obtained the cavity soon becomes lined by a normal polished membrane and shows no tendency to crusting or discharge because of the free drainage; also there is no external deformity; complications are rare; serious burns of the skin seldom result; no instance of spreading osteitis has occurred. Small sequestra and some sloughing are common and as these tend to separate slowly they should generally be removed. Occasionally the sight of the eye may be destroyed or a post-irradiation cataract may develop later. As a rule no treatment of the glands of the neck is required.

The above treatment or some modification of it can safely be carried out for squamous-celled carcinomas, endotheliomas, and low-grade sarcomas, such as the fibro-, myxo-, or chondro-sarcomas, without great risk of dissemination. But when the disease is very advanced and of a highly malignant type it is safer to disturb the growth as little as possible. This question—namely, the risk of dissemination—is very important. It has been suggested that irradiation increases the risk, but I believe that it occurs in many instances before the treatment is commenced.

### INOPERABLE CASES

Undoubtedly many of the growths which we are asked to treat are very advanced and must be regarded as incurable. The highly cellular carcinomas and sarcomas must always be regarded as inoperable. It is a very serious problem to decide whether they should be given any treatment at all. But fortunately many of them are particularly radio-sensitive, so that in practice it is safer to treat them by irradiation alone before attempting to explore them or to remove them surgically. Deep X rays or surface radium, or a combination of both, are probably the safest method of treatment for most cases. Occasionally after preliminary surface irradiation it may be wise to insert a large number of needles into the jaw either through the palate or through the nose. When the growth is very massive long and short needles containing 3, 2, or 1 mg. should be placed uniformly into all parts of it, employing a total of 40 or 50 mg. If heavily screened with 0·8 mm. of platinum they can be left in situ for five to seven days, but the reaction must be watched daily. If this method is adopted a very massive total dose must be given at the risk of a good deal of sloughing and necrosis. And the risk of burns is diminished by using heavy filtration of at least 0·8 mm. of platinum. It is useless to employ smaller amounts. If given boldly, such treatment often gives surprisingly good results. The growth may shrink enormously and some weeks later it may be possible to remove the sloughs, necrotic tissues, and sequestra with diathermy. The following are good illustrations:—

FIG. 3.—Dental plate moulded to fit the cavity in upper jaw and containing radium needles.

Mrs. A, aged 64 (patient of Dr. R. G. Macbeth of Oxford). Twelve months previously a swelling of the left side of the face appeared suddenly and burst inside the mouth. Pain quickly ceased and she had no further trouble for six months, when nose became stuffy and painful. Swelling was noticed on the palate and gradually extended to the upper lip and face. However, she did not consult a doctor for six more months, by which time the growth had ulcerated through the hard palate and through the upper part of the upper lip into the nose. A large fungating mass projected from the nose and the face was greatly swollen.

*Biopsy.*—Squamous-celled carcinoma.

Patient was greatly distressed by pain, stinking discharge, and repeated slight hæmorrhages. The problem which had to be considered was whether any treatment would afford her any relief. With some hesitation she was advised ray treatment starting with nine 30 per cent. doses of deep X rays by Dr. Fairchild. Three days later 24 radium needles—4 × 1 mg., 15 × 2 mg., 5 × 3 mg.—were inserted interstitially into the mass, namely, 49 mg., and retained for one week. Before the week was out 8 needles had dropped out, so that the total dose was approximately 6000 mg. hours—a large amount. Naturally the reaction was severe, but now most of the growth has disappeared. Patient is well and happy and has very little external deformity.

Mr. B, aged 49 (patient sent from Margate by Mr. W. G. Sutcliffe), with a massive tumour of the maxilla causing great swelling of the face and producing a rounded tumour in the mouth in which the upper teeth were completely buried.

*Treatment* consisted of a preliminary course of X rays—about a half dose—followed immediately by a large dose of interstitial radium needles inserted from below.

*Biopsy.*—Cellular carcinoma. Two months later the cavity, which still contained necrotic tissue but very little obvious growth, was cleared by diathermy.

Three years later he was admitted with swelling of the right knee which was twice the size of the left. This

was considered to be a metastasis, and as no other sign of growth could be found either in the jaw or other parts of the body, the limb was treated by X rays. All swelling rapidly disappeared, and in a month he was able to walk comfortably again. Three months later he died owing to metastases in other parts of the body.

Mrs. C, aged 43. Chondro-sarcoma of maxilla. Removed surgically in 1912. Recurrence in 1923. Massive growth in the jaw completely blocking the nose removed by Moure's operation. The growth gradually returned and caused repeated severe hæmorrhages. October, 1924: Patient was much debilitated by bleeding and sepsis. Growth was much larger and caused great deformity of nose and face. A tube of radium containing 100 mg. was inserted into the nose for 24 hours for the arrest of hæmorrhage. Patient's health so much improved that in January, 1925, the whole tumour was stuffed with radium needles retained for a week. This treatment caused great shrinking of the growth, but much sloughing and necrosis. The following May all the necrotic tissue was removed, after which she made a rapid recovery with hardly any deformity. And she has remained well with no sign of recurrence.

## Result

In our cases the combination of treatments has undoubtedly given better results than those previously obtained by surgery and diathermy alone. The prognosis depends upon the nature of the disease, on the stage of its development, and on the previous treatments received. It is often possible to tell beforehand that a case is unfavourable because of its long history and the general debility of the patient resulting in toxæmia and anæmia. It may be assumed as a general principle that these growths are usually very malignant although they seldom metastasise, that most of them have wide extensions into the bones beyond the reach of surgery, and that when they have received treatments elsewhere that they are especially difficult to cure.

### CARCINOMATA

These progress rather slowly as long as they remain intrinsic. As soon as they penetrate the walls of the antrum and begin to involve the subcutaneous tissues, the orbit, the nasal fossæ, or the mouth their growth tends to become more virulent and difficult to arrest. Usually they must be regarded as inoperable, but with irradiation it may be possible to destroy the greater part of the disease or at least to arrest its progress and by shrinking the tumour to stop hæmorrhage, to relieve pain, and to prolong life. But there seem to be some cells which are able to resist even intense treatments and which later slowly recover their vitality, finally becoming completely radioresistant and growing with great rapidity. During the past 15 years we have treated 70 cases with results shown in Table I.

Out of 49 cases of squamous-celled type 19 have died within a year, 6 after two years, 1 after three years, 3 after four years, 1 after six years. The large number who succumbed within the first year are the cases already referred to as being unfavourable for any treatment. The patients living are 14; 6 of them for over five years.

Carcinoma following rodent ulcer shows 8 cases with 6 dead and 2 living. Although this type of disease remains localised and can be temporarily arrested by the above methods, it shows a great tendency to recur. Most of the patients have already received repeated ray treatments with terrible disfigurement and suffering. Our experience of them is so unfavourable that I think that it is doubtful whether a plastic operation to repair the deformity should ever be recommended, even if the disease appears to have been eradicated. Although they may survive for long periods, these types must be regarded as incurable.

With the other forms of carcinomata the numbers are too small to draw any definite inferences. It would seem, however, that the very cellular types respond much in the same way as the rapidly growing sarcomas, and that they can sometimes be cured by ray treatments for long periods; that the spheroidal growths and the peritheliomas are more difficult to cure, likewise the epithelial odontomes, which however may live for longer periods.

As already mentioned, the situation of the disease also has an important bearing upon the prognosis. If the disease is intrinsic it should be possible by drastic treatment to arrest it for long periods in a high percentage of cases, but once it becomes extrinsic or has invaded the upper jaw from outside the prognosis is certainly worse. In those cases where the disease has involved the glands treatment can only be palliative.

### SARCOMATA

The results that have been obtained (Table II.) are surprisingly good. It seems that these types are easier to cure in the upper air-passages than when they occur in other parts of the body, and certainly the credit must be given to irradiation, for surgery

ANALYSIS OF CASES OF MALIGNANT DISEASE OF THE UPPER JAW TREATED AT ST. BART.'S, MOUNT VERNON, AND PRIVATELY

TABLE I

| CARCINOMATA. | Cases. | Dead. | Years. | Lost. | Living. | Years. |
|---|---|---|---|---|---|---|
| Squamous .. | 49 | 30 | 11 in ½<br>8 ,, 1<br>6 ,, 2<br>1 ,, 3<br>3 ,, 4<br>1 ,, 6 | 5 | 14 | 1 for ½<br>3 ,, 1<br>3 ,, 3<br>1 ,, 4<br>1 ,, 5<br>3 ,, 6<br>1 ,, 7<br>1 ,, 8 |
| Rodent ulcer and squamous .. | 8 | 6 | 1 in 2<br>2 ,, 4<br>1 ,, 6<br>1 ,,10<br>1 ,,19 | — | 2 | 1 ,, 2<br>1 ,, 3 |
| Spheroidal .. | 3 | 2 | 1 ,, 1<br>1 ,, 2 | — | 1 | 3 |
| Highly cellular. | 5 | 2 | 1 ,, ½<br>1 ,, 2 | — | 3 | 2 for 2<br>1 ,, 3 |
| Columnar .. | 1 | 1 | 1 | — | — | — |
| Perithelioma .. | 2 | 2 | 2 in ½ | — | — | — |
| Epithelial odontome .. | 2 | 2 | 1 ,, 4<br>1 ,, 6 | — | — | — |
| Total .. | 70 | 45 | | 5 | 20 | |

TABLE II

| SARCOMATA. | Cases. | Dead. | Years. | Lost. | Living. | Years. |
|---|---|---|---|---|---|---|
| Round .. | 6 | 5 | 3 in 1<br>2 ,, 2 | — | 1 | 1 for 7 |
| ,, No biopsy | 5 | 3 | 3 ,, 1 | — | 2 | 2 ,, 2 |
| Spindle .. | 3 | 1 | 1 ,, 5 | — | 2 | 1 ,, 4<br>1 ,,12 |
| Fibro .. | 4 | — | — | — | 4 | 1 ,, 2<br>1 ,, 7<br>1 ,, 9<br>1 ,,10 |
| Myxo .. | 3 | 2 | 1 in ½<br>1 ,, 2 | 1 | — | — |
| Chondro .. | 3 | 1 | 1 ,, ½ | — | 2 | 2 for 1 |
| Angeio .. | 2 | — | — | 1 | 1 | 1 ,, 1 |
| Myeloid .. | 3 | — | — | — | 3 | 1 ,, 4<br>1 ,, 7<br>1 ,,11 |
| Total .. | 29 | 12 | | 2 | 15 | |

TABLE III.—SURVIVAL PERIODS OF ALL THE CASES TREATED

| — | Total | Dead | Lost | Alive | Dead after—(years) | | | | | | | Alive for—(years) | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | —1 | 1 | 2 | 3 | 4 | 5 | 5+ | —1 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 |
| CARCINOMATA .. | 70 | 45 | 5 | 20 | 14 | 10 | 8 | 1 | 4 | — | 2 | 1 | 3* | 2* | 5 | 1 | 1 | 3* | 1 | 1 | — | — | — | — |
| RODENT ULCER +CARCINOMA | — | — | — | — | — | — | 1 | — | 2 | — | 3 | — | — | 1 | 1 | — | — | — | — | — | — | — | — | — |
| SARCOMATA .. | 29 | 12 | 2 | 15 | 2 | 6 | 3 | — | — | 1 | — | — | 3 | 3 | — | 2 | — | — | 3 | — | 1 | 1 | 1 | 1 |
| ENDOTHELIOMATA | 11 | 8 | — | 3 | 3 | 1 | — | 1 | 1 | 1 | 1 | — | — | — | — | — | — | — | — | — | — | — | — | — |
| | — | — | — | — | — | — | — | — | — | After 12 | After 13 | — | — | 1 | — | 2 | — | — | — | — | — | — | — | — |
| Total .. | 110 | 65 | 7 | 38 | | | | | | | | | | | | | | | | | | | | |

* *Lost after:* 1 year, 1 case; 2 years, 1 case; 6 years, 1 case.
*Alive with disease: Less* than 1 year, 2 cases; 3 years, 1 case.

alone is as a rule useless except for a very small group of myeloid tumours.

Out of 29 cases it will be seen that 15 are living for long periods. The fibro- and chondro-sarcomas invariably do well if treated early enough by drastic methods, and seem to show little tendency either to local recurrence or to dissemination. In any case, life can be prolonged greatly but the prognosis is not so good in those who have received previous surgical treatment.

Round and spindle-celled sarcomas, although highly malignant, may also do well. Out of 14 patients treated 5 are living, 2 for over two years, 1 for four years, 1 for seven years, and 1 for twelve years. But these successes are due to the fact that the patients have been treated in most instances by irradiation alone.

Of the patients who have died—12 cases—8 of them have succumbed within a year, mostly from metastases in other parts of the body. There can be no doubt that these rapidly growing types should never be operated upon. Secondary growths in other parts of the body are not invariably fatal. One of our patients was a girl who had a round-cell sarcoma of the nasal fossa and jaw which disappeared after X rays. Three months later she developed a large swelling involving four ribs which was considered to be a secondary deposit. Further treatment by X rays caused the mass rapidly to disappear, and the patient remained well for two years. She was then admitted again suffering from symptoms of acute appendicitis. Laparotomy showed a large mass involving the lower part of the ileum which had perforated. Biopsy proved this to be a round-celled sarcoma. After further X rays the swelling entirely disappeared and the fæcal fistula closed. Now, seven years later, she is in good health and has no signs of her disease.

#### ENDOTHELIOMATA

Out of 11 cases treated, 8 have died, 3 within a year, and 1 each after one, three, four, twelve, and thirteen years; 3 are alive, 1 after two years, 2 after four years. The number of cases treated is so small that one cannot be very definite about the prognosis, and the subject is greatly complicated by the difficulty in classification of these types. But it would seem that those affecting the jaw behave much in the same manner as those in other parts of the body, that the best results can be obtained by combination treatments including pre- and post-operative X rays or radium, and that certainly all of them are radio-sensitive excepting the recurrent tumours which often take on a very virulent form of growth and become resistant to rays. With combined methods one ought always to obtain an arrest of the disease for long periods and in early cases a large proportion of permanent cures.

### Conclusion

I think it is fair to say that the combined treatment is giving us good results and that cancer of the upper jaw is easier to cure than in any other part of the upper air-passages with the exception of the larynx. But it should be remembered that there is one good chance of curing this disease so that it should be treated early and with every known weapon that exists. When considering the figures it must be emphasised that a large percentage of our cases have been very advanced, some of them hopeless, so that treatment was only given for palliation—in fact one may say that we have only refused treatment to those who were too debilitated to tolerate it, never because the disease was too advanced.

Table III. shows at a glance the survival periods in the whole series. In spite of the unfavourable nature of the cases it will be seen that (1) nearly a third of the carcinomas are living, 2 for two years, 5 for three years, 1 for four years, and 6 for five years or more; (2) half the sarcomas are alive and those who survive for more than one year usually remain free from disease for long periods; (3) although only 2 of the endotheliomas are now living, 4 others survived for over three years.

Actually the results are better than the tables suggest because in many of the patients who are dead the growths were temporarily arrested and their symptoms were enormously relieved.

Undoubtedly in recent years our results have been better because we have improved our treatment by irradiation, and as we learn more about this subject it is reasonable to hope that still better results may be obtained.

I should like to thank for advice, criticism, and help on innumerable occasions my colleagues, particularly Dr. N. S. Finzi, Dr. W. M. Levitt, and Dr. R. G. Canti, at St. Bart.'s, Sir Cuthbert Wallace, Mr. S. Cade, and Dr. G. C. Fairchild at Mount Vernon.

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SMOKELESS HOUSES AT OLDHAM.—A group of 900 six-roomed houses which are being erected at Chadderton, near Oldham, will, it is stated, be the first entirely smokeless estate in this country. The building of 1500 similar houses has been started at Unsworth, Bury, Lancashire.

KING EDWARD HOSPITAL FUND FOR LONDON.—Amongst the latest contributions to King Edward's Hospital Fund are £1000 from the King, who is patron of the fund, and 100 guineas from the Queen.

In aid of the Fund four personally conducted tours have been arranged, beginning with a visit to Cadby Hall, conducted by Sir Isidore Salmon, M.P., at 2.30 P.M. on Jan. 25th. The other places to be visited will be the *Daily Telegraph* office (10.30 P.M. on Feb. 6th), the Houses of Parliament (Feb. 20th), and Westminster Abbey (March 13th). Particulars may be had from the secretary at 10, Old Jewry, E.C. 2.

# OBSERVATIONS ON RICKETS

By Wilfrid Sheldon, M.D., F.R.C.P. Lond.

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Within the last decade the identification of vitamin D and of its rôle in the prevention of rickets has led to a rapid diminution of the incidence of this disease, to such an extent that rickets is fast becoming an uncommon condition, and the medical student of to-day may consider himself fortunate if he sees as many as half a dozen cases during his period at hospital. Moreover, the cases that come his way will but seldom show the galaxy of signs that have been so beautifully described in the older text-books, such for instance as enlargement of the epiphyses, bossing of the skull, bending of the long bones, and pot-belly. These signs are only apparent when the disease is already well advanced, and at the present day therapeutic measures will almost certainly have been adopted before such a stage is reached. The disease as it is now met with is more likely to be seen in its incipient stages and in young infants, and a knowledge of the early signs is more than ever necessary if cases are to be recognised and treated at the earliest opportunity.

## SIGNS

The early signs are easily overlooked unless a specific examination is made for each of them, for as a rule the infant is well nourished and at first sight may appear healthy. It has been the usual teaching that rickets is most commonly met with between 6 and 18 months of age, but at the present day most of the cases arise during the first year, and may sometimes be detected as early as the third month.

*Craniotabes.*—The onset is insidious, and although such early symptoms as sweating about the head, restlessness, and irritability are suggestive, they are not sufficient by themselves to establish the diagnosis. Probably the earliest skeletal sign is craniotabes. Hess found this sign to be present in 93 out of 200 infants under four months of age, and in 28 out of 89 infants between four and six months, but a most careful examination of the skull must be made if this sign is not to be overlooked. The infant's head should be held cupped in the examiner's hands while the finger tips make careful and firm palpation over the back of the head low down along the parieto-occipital suture, since this is the place where craniotabes first appears. When this sign is present, one or more small circumscribed areas of the skull can be indented just as can a rubber ball, the bone rebounding into position when the pressure of the finger is released. "Egg-shell crackling" is not likely to be felt unless the rachitic process is severe and extensive.

Although craniotabes is a very valuable sign of early rickets, it may occur in other diseases, and therefore is not necessarily diagnostic of rickets. It is a good rule not to diagnose rickets on the occurrence of only one physical sign, and this is as

TABULATED SERIES OF ELEVEN RACHITIC INFANTS TREATED DURING THE FIRST QUARTER OF 1934

| Case No. | Age of onset. | Prematurity. | Diet. | Whether put out of doors. | Clinical evidence of rickets. | Radiological evidence. | Blood phosphorus (mg. per 100 c.cm.) | Calcium (mg. per 100 c.cm.) | Complications. |
|---|---|---|---|---|---|---|---|---|---|
| 1 | 11 wks. | 1 mo. | Breast then milk and water. | Not out of doors. | Cran. and slight beading. | Negative. | — | — | — |
| 2 | 14 wks. | Full term. | Breast 9 wks. then dried milk. | Out of doors since 7 wks. | Cran. and beading of ribs. | ,, | — | — | — |
| 3 | 4 mos. | 1 mo. | Breast. | 15 hours each week. | Cran. and slight beading. | Indefinite. | — | — | — |
| 4 | 5 mos. | Full term. | Breast and dried milk. | ? | Two fits at 7 wks.; cran. and beading of ribs. | Slight at lower end of ulna only | — | — | — |
| 5 | 5 mos. | ? | Dried milk. | Not out of doors. | Cran.; beading; big fontanelle. | Indefinite. | — | — | Broncho-pneum. |
| 6 | 5 mos. | Full term. | Nestlé's. | Not taken out every day. | Fits; laryngospasm; anæmia; beading; cran.; big fontanelle. | Negative. | 5·7 | 6·1 | — |
| 7 | 5½ mos. | ,, | Breast 5 wks. then quaker oats and semolina. | ? | Cran.; beading of ribs; Chvostek's sign. | Slight at lower end of ulna and tibia. | 4·9 After 5 days' treatment. | 8·3 | Eczema. |
| 8 | 6 mos. | 2 mos. | Breast then milk and barley-water | Out of doors most days. | Two fits; laryngo-spasm; Trousseau's sign; cran.; beading of ribs. | Definite at wrist and ankle. | 6·4 | 4·2 | — |
| 9 | 7 mos. | ? | Nestlé's. | ? | Cran. and beading of ribs. | Slight at lower end ulna only. | 5·2 After 9 days' treatment. | 9·5 | Lobar pneum. |
| 10 | 7 mos. | 3 wks. | Groats and Nestlé's. | ? | Cran.; beading; anæmia. | Gross changes wrist and ankle. | 3·1 | 8·9 | — |
| 11 | 9 mos. | 2 mos. | Sister Laura food 5 mos. and milk and water. | Not taken out. | Cran.; big fontanelle; beads; enlarged epiphyses. | Gross changes. | — | — | Scurvy; broncho-pneum. |

Cran. = craniotabes.

true for craniotabes as for other signs. Confirmatory evidence should always be required. Digital pitting of the skull can also be obtained in some instances of hydrocephalus, and in the rare condition of osteogenesis imperfecta; it has also been thought to be a sign of congenital syphilis, although it is probable that in such cases rickets is present as an associated condition. There is no doubt that craniotabes may occasionally occur in very young infants who show no other trace of disease, especially in infants born prematurely, but such physiological craniotabes generally disappears in a few weeks.

There may sometimes be considerable difficulty in determining how much significance shall be given to craniotabes. This was so in two infants seen during last spring.

One was a full term male child, 9 weeks old, who had been reared on Nestlé's milk and had been taken out of doors each day. The craniotabes was easily elicited in the region of the lambdoidal suture, but there were no further signs of rickets, the blood calcium and phosphorus were normal (10·1 and 6·9 mg. per 100 c.cm. respectively), and radiogram of the wrists was also normal. The baby was put on to a dried milk and given irradiated ergosterol, and the craniotabes gradually disappeared in a month.

The other was a girl, aged 5 months, born one month prematurely, but breast-fed and put out in the garden every day. She had craniotabes such as would have been considered typical of rickets, but there were no other clinical signs, radiography of the wrists was normal, and the blood calcium and phosphorus were normal (11·0 and 5·7 mg. per 100 c.cm. respectively). She was given calcium lactate and irradiated ergosterol. Ten days later she had two convulsions for no very obvious reason. At first these fits were thought to be spasmophilic, but there were no traces of tetany or laryngospasm and another estimation of the blood calcium and phosphorus gave a normal result (11·7 and 4·7 mg. per 100 c.cm. respectively). Although antirachitic treatment was continued and the craniotabes disappeared in three weeks, it was not at all clear in either this or the preceding case that the craniotabes was more than physiological.

*Beading of ribs.*—The other early skeletal sign is beading of the ribs, which may be found as early as the fourth month, although at this age the beads will have to be felt for, as they will not yet be visible. They are most easily felt at the fifth, sixth, and seventh chondro-costal junctions just below and outside the nipples. At this stage, swelling of the epiphyses cannot be made out, nor will there be any bending of the long bones, while the size of the fontanelle in such young infants will be a quite unreliable guide.

The *radiographic* changes occurring at the ends of the long bones in rickets are so typical that when any doubts of the diagnosis arise, they may be quickly dispersed by an X ray examination. The changes consist of a broadening and hollowing out of the end of the bone with a frayed appearance at the epiphyseal line. The first bone to show such changes is the ulna at its distal end, and for this reason the wrist is the joint usually selected for this investigation. It should, however, be borne in mind that craniotabes and beading of the ribs—the two earliest skeletal signs of rickets—may both be detectable and permit of the diagnosis being made before X ray evidence can be made out.

## BIOCHEMICAL CHANGES IN RICKETS

The metabolic disturbance in rickets chiefly concerns calcium and phosphorus, the amount of either one or the other being lowered in the circulation, while occasionally both are lowered simultaneously. It is permissible to speak of two biochemical types of rickets, the low phosphorus type and the low calcium type, and of these the former is the more common. These types can often be distinguished clinically, for an infant with the low calcium type may exhibit one or more of the triad of symptoms grouped together as "spasmophilia"—namely, tetany, laryngismus stridulus, and convulsions, all of which depend upon a low blood calcium, while an infant with the low phosphorus type but with a normal amount of circulating calcium will not show these manifestations. If the symptoms of spasmophilia accompany rickets, they will do so in its early stages, and may be present before the sixth month and before X ray changes can be made out. The occurrence of convulsions in an infant over three months of age should always prompt an examination for the early skeletal signs of rickets and for other signs of spasmophilia.

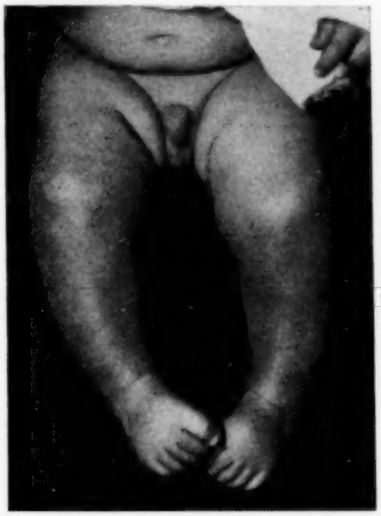

FIG. 1.—Non-rachitic bowing of the legs in an infant one year old.

Other effects of rickets upon the soft tissues, such as laxity of ligaments and joints, atony of muscles, splenic enlargement, and abdominal distension, are seldom early manifestations, appearing as a rule during the second year; but, as Still has pointed out,[1] they may occasionally take a more prominent place in the clinical picture than the skeletal changes. There is one symptom which may, however, occur early, and that is anæmia.

The particular tendency of infants born prematurely to develop rickets has long been recognised, and for them measures of prevention need to be started soon after birth and steadily maintained if the disease is not to occur. On this account it is likely that with the increasing prevention of rickets in general, a relative preponderance of cases will appear in premature infants.

## A SERIES OF CASES

The various points outlined above are well illustrated by a consecutive series of eleven rachitic infants treated in the children's department of King's College Hospital during the first quarter of 1934. The details are set out in the accompanying Table.

*Age.*—The average age of these eleven infants was a little over 5 months. The youngest was 11 weeks,

[1] Still, G. F.: Common Disorders and Diseases of Childhood. London. Fourth edition. 1924.

seven of the cases were under 6 months, while the oldest, a quite exceptionally severe case, was 9 months. This age-incidence is decidedly lower than the usual statement of 6–18 months.

*Prematurity.*—Inquiry as to prematurity was made in nine of the cases, five of which were born prematurely.

*Diet and sunlight.*—The new knowledge of vitamin D has taught us that an infant has a twofold source of this vitamin, one obtained from the diet, and the other from the manufacture of the vitamin in his

FIG. 2.—Radiographic appearance of the legs shown in Fig. 1.

skin after he has been exposed to ultra-violet light—derived from sunlight or from an ultra-violet lamp. In any given case of rickets the summation of these two sources must be reckoned with in determining why there has been a lack of vitamin D. With regard to breast milk, although it is usually protective against rickets, its antirachitic value will depend upon the amount of vitamin D in the maternal diet together with the amount of ultra-violet light to which the mother is exposed. When these two factors are deficient the milk will no longer protect against rickets.

In the present series only one infant (Case 3) was entirely breast-fed, and this baby was also out of doors for roughly 15 hours each week. The rickets was attributed largely to the fact that the infant was prematurely born, and it is also probable that the antirachitic value of the breast milk was poor, for the infant was treated successfully by exposing the mother to ultra-violet light. One other child was receiving breast milk supplemented with a dried milk, and developed a slight degree of rickets at five months. The remainder were being fed artificially at the time of onset of the disease, and direct questioning in six of these showed that three were not being taken out of doors at all, while another was "not taken out every day." Although it is likely that in this country during the winter months the mere fact of having an infant out of doors during the day will not be sufficient to protect entirely against rickets, it is nevertheless a valuable aid in preventing the disease at a time when the content of vitamin D in fresh foods is at its lowest.

*Physical signs.*—The two outstanding signs were craniotabes and beading of the ribs, which occurred in every case. It must be emphasised, however, that neither of these signs would be apparent in any cursory examination, since only in the last case was the beading sufficient to be at once obvious on inspection, while of course no amount of inspection would reveal craniotabes. The fontanelle seemed larger than normal in three cases, and one infant was considerably anæmic. With the exception of the last and most severe case, enlargement of the epiphyses could not be made out, nor was there any suggestion of bending of the long bones. Four of the infants showed one or more signs of spasmophilia, and so were judged to belong to the low calcium type of rickets; biochemical investigation was made in three of these (Cases 6, 7, and 8), and confirmed the low value of the blood calcium, which in one instance reached the remarkably low figure of 4·2 mg. per 100 c.cm.

*X ray findings.*—It was possible to confirm the statement already made that X ray evidence of rickets does not offer the earliest means of diagnosis, being sometimes preceded by craniotabes, beading of the ribs, and symptoms of spasmophilia. Only three cases, aged 6, 7, and 9 months, showed sufficient changes on the X ray films to be of real diagnostic value; three cases showed slight changes at the lower end of the ulna, the appearances being only enough to support, without proving, the presence of rickets; while in five cases the bones were either normal or the changes too indefinite to be of any help, and these cases were all below six months of age.

*Treatment* consisted of giving cod-liver oil and/or irradiated ergosterol, together with exposure to ultra-violet light. In one instance the mother, who was feeding her infant, was irradiated, with a good result. Two of the infants died, one from pneumonia and empyema, the other was admitted moribund with scurvy and broncho-pneumonia.

### NON-RACHITIC BOWING OF THE LEGS

It frequently happens that an infant is referred to hospital with the diagnosis of rickets already made on account of bowing of the legs, but the mere fact that an infant seems bandy does not of itself justify a diagnosis of rickets. It should be remembered that bowing of the legs when due to rickets is a relatively late sign, arising at the end of the first year or during the second year, and it is always accompanied by other manifestations of the disease. Hess has pointed out [2] that bowing is often present in the new-born, which he attributes to a cramped position in utero, and he also remarks on the bowing which may occur in robust healthy babies without any evidence of rickets, and states that a non-rachitic type of genu varum must be recognised. The appearance of bowing in these cases is due in part to the accumulation of fat on the outer side of the leg, accentuated by the natural varus position of the feet, and persists until well into the second year when the child is reaching the toddling stage. As regards the tibia, any curvature is often more apparent than real, for X ray examination generally shows the bone to be straight (see Figures). Moreover, the appearance of the legs is different in the two cases, for the non-rachitic type of curving is a gentle one affecting nearly the whole length of the leg from the knee down, while the rachitic curve affects chiefly the lower third of the leg, and the lower

[2] Hess, A. F.: Rickets, Tetany, and Osteomalacia. London. 1930.

end of the rachitic tibia is curved backwards as well as inwards.

This not infrequent error will be avoided if other signs of rickets are insisted upon in addition to bandy legs. It may be added that there is nothing to be gained by attempting to keep children with non-rachitic curvature "off their legs," for the bones are amply strong enough to support the child's weight; in fact no treatment is required, as the appearance of bowing passes off during the second year.

In conclusion my thanks are due to Dr. R. A. McCance, who kindly carried out the biochemical investigations for me.

SUMMARY

(1) The earliest skeletal changes of rickets are craniotabes and beading of the ribs, and both may precede radiological evidence of the disease. Symptoms of spasmophilia may also be among the earliest indications. (2) These findings are illustrated by a consecutive series of 11 cases of rickets. (3) A non-rachitic form of bowing of the legs is described. It is commonly present in infancy, and is apt to be mistaken for rickets.

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# IMMUNISATION AGAINST DIPHTHERIA

## BY MEANS OF A SINGLE DOSE OF ALUM-PRECIPITATED TOXOID (A.P.T.)

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IT is generally recognised that the efficiency of a diphtheria prophylactic depends not only upon the antigenic value of the toxin employed, but also upon the rapidity with which the antigen is absorbed from the site of injection. One dose of a prophylactic which is rapidly absorbed and eliminated leads only to a small increase in antitoxic titre of the serum, and to produce a sufficiently high immunity repeated doses are necessary. Consequently high value formol toxoids, which have been shown (see O'Brien and Parish,[1] Parish,[2] and Underwood[3]) to be exceedingly effective when given in the usual multiple doses, are unsuitable for use as single-dose prophylactics because the rate of absorption is too great to provide a continuous stimulus over a period of time. For example, Tron[4] used a single dose of unconcentrated formol toxoid, equivalent to 80–100 Lf units given at one injection, on a series of 110 children. One month after the injection 49·09 per cent. were Schick-negative, and two months after the injection only 57·2 per cent. were negative. These results are more or less in accord with my own (unpublished) results obtained with single doses of high-value toxoids; and with those of White and Schlageter,[5] who found 49·2 per cent. of children, inoculated with a single dose of toxoid, Schick-negative in two months, and 82 per cent. in six months. Quite recently it has come to be realised that these intervals are much too long for any practical scheme of immunisation.

The work of Glenny and his colleagues (see [6] and [7]) showed that it was possible to precipitate the active factors of certain toxoids by means of alum, and that these precipitates possessed very high antigenic properties, with the additional advantage that the precipitate was absorbed slowly from the tissues. Glenny and his co-workers[7] suggested from their experimental work in animals that, when an antigen is injected into the tissues, a condition of continual stimulation is produced "by lessening quantities of antigen acting on tissues whose power of response is rapidly increasing." They further suggested that the action of the alum was to retain the antigen in the tissues until these had acquired the power of responding rapidly to the stimulus. Saunders[8] in Cork showed that alum-toxoid (A.M.T.) was a very efficient immunising agent when employed in three doses. A disadvantage in using it is the possibility of the occurrence of subcutaneous abscesses due to the retention of the alum in the tissues. In Saunders' series of 579 cases, subcutaneous abscesses were met with four times.[9]

The obvious advantages of a prophylactic which would induce immunity by means of a single dose led certain workers to try alum preparations for this purpose.

Jensen[10] inoculated 21 children, each child receiving 1 c.cm. of formol toxoid concentrated by alum. The resulting preparation had an Lf value of 150 per c.cm. One month after the injection 20 of the children had become Schick-negative. Graham, Murphree, and Gill[11] used an alum-precipitated formol toxoid, prepared after the method of Glenny. A single inoculation was given to 185 children who were all Schick-positive. When tested two to six months later 171 (92·4 per cent.) of the children had become Schick-negative.

Underwood[12] reported the results of a single dose of formol toxoid *plus* alum—i.e., not precipitated alum toxoid A.P.T.—on 59 Schick-positive children. (*a*) Of 17 Schick-positive children, 8 were Schick-negative four weeks after the injection and 12 were negative six weeks after the injection; the percentages negative were thus $47·0 \pm 8·2$ and $70·6 \pm 7·5$ respectively. (*b*) Of 22 children in another batch, 9 were negative four weeks after injection—i.e., $40·9 \pm 7·1$ per cent. (*c*) Of 20 boys, aged 15 to 18 years, 17 were negative four weeks after injection—i.e., $85·0 \pm 5·4$ per cent. The probable errors showed that these results in this small series were statistically significant.

Baker and Gill[13] employed alum-precipitated toxoid on 197 Schick-positive children. The second Schick test was carried out at intervals varying from six weeks to six months after the single injection, the average time being two to three months, and all the children had become negative to the test before the end of this period. Straus[14] recently obtained good results with a toxoid made up in a special lanoline mixture.

### RESULTS OF INOCULATION WITH A.P.T.

It is evident from what has been written that there is a prima facie case for further experimental work on alum-treated toxoids, with a view to the development of an efficient and safe prophylactic when used in single doses. Through the courtesy of Dr. R. A. O'Brien, director of the Wellcome Physiological Research Laboratories, I investigated such preparations over a considerable time in Leeds. The previous communication[12] dealt with preliminary work, and numerous cases have now been treated with alum preparations. The object of the present paper, however, is merely to indicate the degree of success which has been obtained with the most recent preparation—an alum-precipitated toxoid (A.P.T.) of high antigenic value. This material had been treated according to a method worked out by G. C. Pope which removed a large proportion of inactive material, and was expected to produce much less reaction than previous preparations. The method is to be the subject of a further communication by Pope and his colleagues.

As a preliminary to a review of these results it must be reiterated that, for reasons which cannot be dealt with in this paper, the Leeds children are exceptionally difficult to immunise. For further details reference should be made to a previous communication.[3] I should like, however, to add here that recent work in London has convinced me that my former observations on this point were correct. The inference is that similar work, carried out in many other parts of the country, would have yielded even better results.

The material for the investigation consisted of 228 children, divided into five batches, which are here labelled $\alpha$ to $\epsilon$. The ages of the children ranged from 1 year to 14 years, but the majority were between 1 and 5 years of age. Particulars of the Schick-state of these children are given in Table I.

TABLE I

| Batch. | Number tested. | Negative. |
|---|---|---|
| $\alpha$ | 47 | 12 |
| $\beta$ | 53 | 16 |
| $\gamma$ | 36 | 3 |
| $\delta$ | 48 | 13 |
| $\epsilon$ | 44 | 5 |
| Totals | 228 | 49 |

Each child received preliminary Schick and Moloney tests, and the Schick-positive, Moloney-negative reactors were each given 1 c.cm. of A.P.T. (Batch B9017) subcutaneously in the left deltoid region. Of the cases so treated it was practicable to perform a final Schick test on 152 four weeks after the injection. The results in this paper are therefore based on these 152 cases. Table II. summarises these results.

TABLE II

| Batch. | Number finally tested within 1 month after single dose. | Negative after 1 month. | Per cent. negative. |
|---|---|---|---|
| $\alpha$ | 29 | 22 | $75{\cdot}9 \pm 5{\cdot}4$ |
| $\beta$ | 25 | 24 | $96{\cdot}0 \pm 0{\cdot}8$ |
| $\gamma$ | 28 | 23 | $82{\cdot}1 \pm 4{\cdot}9$ |
| $\delta$ | 33 | 26 | $75{\cdot}8 \pm 4{\cdot}8$ |
| $\epsilon$ | 37 | 32 | $86{\cdot}5 \pm 1{\cdot}2$ |
| Totals | 152 | 127 | $83{\cdot}6 \pm 2{\cdot}0$ |

Since the probable errors, not only for the collected results but also for the results for each individual batch, show that these figures are highly significant, it would seem that the investigation has yielded a very promising line of inquiry. It is true that the figures for individual batches show some variation, and the probable errors of certain differences suggest that these differences are probably significant. Hence too much stress should not be placed on the figures for individual batches. Apart from this, however, the results as they appear in Table II. require further examination.

TABLE III

| Age-group | Under 1 | —2 | —5 | —7 | —10 | 10+ |
|---|---|---|---|---|---|---|
| Total tested | 11 | 27 | 57 | 18 | 20 | 19 |
| Results of tests— | | | | | | |
| (*a*) Positive | 2 | 2 | 9 | 2 | 4 | 6 |
| (*b*) Negative | 9 | 25 | 48 | 16 | 16 | 13 |
| Per cent. negative. | 82 | 93 | 84 | 89 | 80 | 68 |

(*a*) In the first place, there is a possibility that the high percentage of negative reactors on re-testing may have been due to the inclusion of an unusually large number of children at one particular age. A rough idea of the results as related to the age-distribution is given in Table III. (*Note.*—In Tables III. and IV. only the 152 children included in column 2 of Table II. are dealt with.)

These figures indicate in a broad way that up to the age of ten years there was no marked difference in the immunising effect of the prophylactic. Children over ten years were apparently rather more difficult to immunise by this method. At all events the figure $83{\cdot}6 \pm 2{\cdot}0$ must be taken as representative of the average percentage of children in any age-group who would, in the Leeds district, be made immune within one month of the administration of a single dose of the prophylactic.

(*b*) In the second place, the figures in Table II. give no indication of the state of immunity of the 152 Schick-positive subjects before inoculation. It might be objected that possibly many of the children had a considerable degree of immunity to start with—i.e., the positive Schick reaction would be slight in degree—and that therefore a small stimulus would be sufficient to induce effective immunity and to change the slight positive into a negative Schick reaction. This point is dealt with in Table IV., which gives the initial Schick-state and the effect of inoculating the 152 cases.

TABLE IV

| Primary Schick. | | Final Schick (1 month after inoc.). | | Per cent. neg. 1 month after inoc. |
|---|---|---|---|---|
| Type. | Number and per cent. | Positive. | Negative. | |
| Slight | 16 (10·5) | 1 | 15 | 93·8 |
| Moderate | 97 (63·8) | 15 | 82 | 84·5 |
| Marked | 39 (25·7) | 9 | 30 | 76·9 |
| Total | 152 | 25 | 127 | — |

As would be expected, there is a difference in the ease with which the three groups can be immunised, but the difficulty is obviously progressive, and the difference in the percentages for "slight" and for "marked" groups respectively is not as great as might have been anticipated. It is noteworthy that the percentage of "marked positive" Schick reactors in this group of children is considerably higher than I found in a larger sample of the Leeds child population (see, for example, ref. 3). The outstanding points which emerge from this Table are that the average percentage of children Schick-negative after one month—viz., $83{\cdot}6 \pm 2{\cdot}0$—is a representative figure for "moderate" and for "marked" primary Schick reactors; and further, that almost 80 per cent. of "marked" Schick reactors can thus be rapidly immunised by this method.

It should be mentioned that I followed my usual practice of reading as "positive" all Schick reactions in which there was the slightest suspicion of erythema. As a consequence of this procedure one case is included as "positive" in the above figures for the final Schick tests, although the result of blood titration showed that the patient was immune at the time when the Schick test was carried out.

### REACTIONS

It has been pointed out that the degree of reaction must always be discussed in any communication dealing with alum toxoids. In all of the cases in the present series the arms were examined for reactions

on the day following the injection. If necessary the cases were seen again later. The reactions were classified into three types: (*a*) general reactions, such as fever, vomiting, nausea, headache; (*b*) erythema at the injection site; (*c*) induration at the injection site. Information under each of these three headings was elicited in every case.

In the present communication it is not proposed to discuss these reactions fully, but the following brief summary will indicate what is to be expected with this material. This information is available for 161 cases, each of which received a dose of 1 c.cm. In the Moloney-negative cases general reactions were practically absent. A few children showed slight lassitude or nausea, and slight stiffness of the arm was a not uncommon complaint. Erythema, which was so faint as to be barely distinguishable, was seen in 30 cases. In 16 other cases the erythema was somewhat more marked—e.g., an area up to 20 mm. in diameter. Localised subcutaneous induration is, of course, to be expected in many cases after the injection of an alum preparation. The commonest type is that which is apparent to the touch as a small pea in the subcutaneous tissues. This type of induration occurred in 37 cases. Apart from this, slight generalised induration was seen in 13 cases.

It will be apparent that in this series the reactions were very mild and caused no anxiety whatever. It should be mentioned, however, that I have since seen two cases in which the reactions were of quite a different type. In both there was a diffuse brawny induration of the skin of the upper arm, with increase of local heat and some hardening of the tissues.

Certain Moloney-positive reactors (not included in Table II.) were given small doses of the material. Of nine such cases, ages 7 to 11 years, after one dose of 0·3 c.cm. six showed more or less definite general reactions, such as vomiting and headache; five showed redness of greater intensity than was observed in Moloney-negative cases (say up to 30 mm. in diameter); and three showed definite general induration around the injection site. It is obvious, therefore, that it is essential when these materials are to be used, not only to perform the Moloney test, but to interpret it strictly. I have on several occasions laid emphasis on this line of procedure. A further corollary is that this work should only be performed by persons who have had some experience of the Moloney test and of the reactions which may be elicited by strong toxoids in Moloney-positive reactors.


### SUMMARY

A potent batch of alum-precipitated toxoid was tested on five groups of children, all of whom were Schick-positive before inoculation. Each child received one dose (1 c.cm.) of this material, and in 152 cases a final Schick test was performed one month after the injection. It has been shown that the figure $83{\cdot}6 \pm 2{\cdot}0$ represents the average percentage of children who became Schick-negative within four weeks. The reactions were classified into three types—general, local erythema, and local induration. Generally these reactions were very mild; but the occurrence of much more severe reactions in two cases shows that due care must be exercised in this work, and emphasises the necessity for a strict interpretation of the Moloney test.


I am indebted to Dr. R. A. O'Brien, of the Wellcome Research Laboratories, for his kindness in supplying the material and for his interest in the investigation.

(*References at foot of next column*)

# INDICATIONS FOR THE CLINICAL USE OF PROGESTIN

## STANDARDISED CORPUS LUTEUM EXTRACT


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HITHERTO the supplies of a reliable corpus luteum extract have been so scarce in this country that its use as a therapeutic agent could not be evaluated. It is hoped that in the near future a synthetic process of preparation will be satisfactorily elaborated and thus reduce the cost and increase the amount available for clinical trial.

Through the courtesy of Organon Laboratories a certain amount of Progestin has been put at our disposal for use at the Endocrine Clinic attached to the Gynæcological Department of Guy's Hospital, and though the number of cases in which it has been employed is as yet too small to warrant a detailed clinical report, we have been favourably impressed with its value in certain disorders of menstruation and pregnancy. The purpose of the present communication is to indicate the underlying principles by which we have been guided in our use of progestin, in the hope that it may be of assistance to those who have hesitated to use the product on account of its expense and the lack of any well-defined indications and of published clinical results.

### THE RÔLE OF PROGESTIN IN THE NORMAL MENSTRUAL CYCLE AND IN PREGNANCY

The activity of the ovary is regulated by endocrine factors secreted by the anterior lobe of the pituitary gland. These are responsible for stimulating the development of the Graafian follicle and the secretion of the follicular hormone œstrin, and for inducing rupture of the follicle and the appearance of the corpus luteum, which not only continues to secrete œstrin, but also elaborates its own specific hormone, progestin.

The ovary, in its turn, regulates the changes which occur in the uterus, both during the normal menstrual


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cycle and in pregnancy. During the time before ovulation when only œstrin is being secreted by the ovary the uterine endometrium is in the proliferative phase. Its glands are long and tubular and secretion is almost absent. Its stroma consists of undifferentiated fibrous connective tissue. With the appearance of the corpus luteum and the secretion of progestin after ovulation the character of the endometrium alters. The glands become spirally twisted and produce a fair amount of mucous secretion, and the stroma is converted into decidua, which is the characteristic feature of this stage of the menstrual cycle and of early pregnancy. This second half of the menstrual cycle is known as the progestational phase. It is dependent for its appearance on the secretion of progestin by the corpus luteum (see Fig. 1).

The ovary is also responsible for the changes which occur in the uterine muscle. The growth and development of the uterus to adult proportions are dependent on the adequate secretion of œstrin by the ovary. The uterine muscle is inherently contractile, and responds to small doses of the oxytocic factor of the posterior lobe of the pituitary. This represents the condition of the muscle during the first half of the menstrual cycle, but with the appearance of progestin the muscle loses its excitability and much larger doses of oxytocin are required to effect a response. In other words, progestin inhibits the spontaneous activity and responsiveness of the uterine muscle to oxytocin.

The combination of a progestational type of endometrium and a quiescent uterine muscle is an ideal state for the nidation of the fertilised ovum in the uterine cavity. Once the placenta is fully developed, at the end of the third month of pregnancy, the fœtus is comfortably established in the uterus and the influence of the corpus luteum is no longer necessary. It consequently atrophies and disappears by the end of the first half of pregnancy.

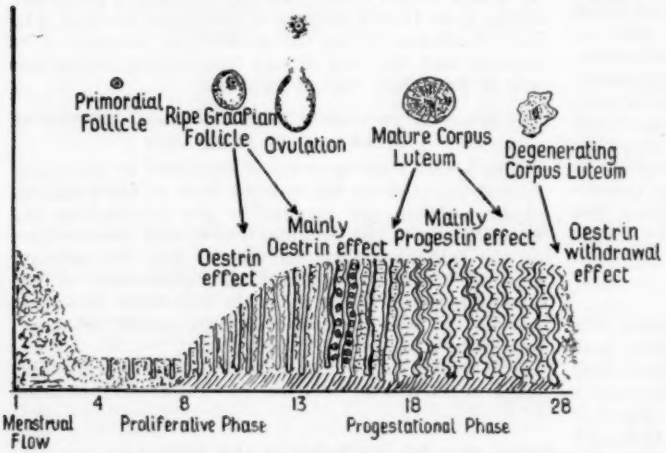


FIG. 1.—The inter-relations of the ovarian and menstrua cycles.

Fig. 2 illustrates the scheme of interaction of the hormones, upon which is based the indications for the use of progestin.

### EFFECT OF PREMATURE WITHDRAWAL OF PROGESTIN (FIG. 3)

The corpus luteum normally reaches full development on about the nineteenth day of the menstrual cycle, and from then onwards gradually regresses until it finally ceases to function on the twenty-eighth day of the cycle or the first day of the next period. During this time, under the influence of progestin, the uterine muscle remains quiescent. It has been suggested that should the progestin influence be removed prematurely—i.e., two or three days before the menstrual flow commences—the uterine muscle would be released from the inhibitory effect of progestin and might undergo comparatively violent and painful contractions, giving rise to dysmenorrhœa, especially that type associated with two or three days' premenstrual pain. On this theory it would be logical to treat such cases of functional dysmenorrhœa with progestin for a few days before the onset of the menstrual flow. We have employed this treatment in a few cases of dysmenorrhœa, in some of which it has been effective where other methods have failed.

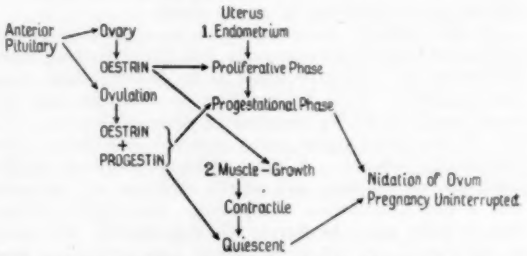


FIG. 2.—The influence of the anterior pituitary on the ovary and of the ovary on the uterus.

Premature withdrawal of progestin may also occur in pregnancy, when the corpus luteum begins to degenerate before the end of the third month. In these cases the uterine muscle once more becomes contractile, and the decidual reaction, which is so essential to the embedding of the ovum and development of the placenta, begins to disappear. The embryo now has a very insecure foothold in the uterus, and abortion is likely to occur. This is the underlying cause of those cases of habitual abortion for which no organic lesion can be held responsible. The miscarriage usually occurs within the second or third month of pregnancy. Treatment of these cases with progestin during this critical period should serve to preserve the decidua and inhibit the motility of the uterine muscle, so that the pregnancy is maintained until after the third month when the placenta is fully developed.

### EFFECT OF INADEQUATE STIMULATION OF THE OVARY BY THE PITUITARY (FIG. 4)

The pituitary may fail to produce sufficient secretion to stimulate ovulation of the ripe Graafian follicle. This will consequently continue to grow and a follicle cyst may be formed. From this œstrin will continue to be secreted. This œstrin will stimulate an exaggerated proliferative type of endometrium, but owing to the absence of progestin the progestational phase will not be reached.

It has been found that if large doses of œstrin are given to castrated monkeys, uterine hæmorrhage occurs a few days after the administration is discontinued. In this experiment the large doses raise the œstrin concentration to a high level. *When this level begins to fall*—on discontinuing the œstrin

administration—uterine hæmorrhage commences. It will be noticed that this bleeding occurs in the complete absence of a corpus luteum.

In the same way, clinically, the amount of œstrin secreted by follicular cysts, though high, is subject

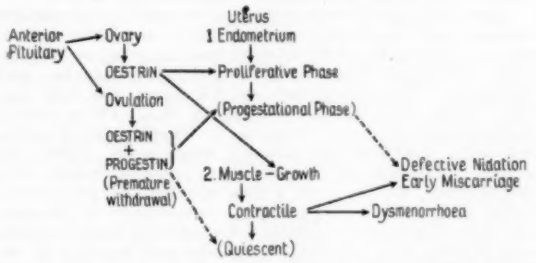


**FIG. 3.**—The effect of premature withdrawal of progestin.

to fluctuations, with a tendency to uterine hæmorrhage, which may take the form of a pure menorrhagia or of a metrorrhagia. The uterus is usually of normal size, or even larger in some cases, its growth and development being stimulated by the œstrin secreted from the follicular cysts. The motility of the muscle, however, is not subjected to any inhibitory influence, and some of these cases of menorrhagia are associated with dysmenorrhœa.

The primary indication in this condition is to stimulate ovulation by the administration of anterior pituitary preparations, but this treatment may be supplemented by giving progestin, particularly during the actual bouts of bleeding. This antagonises the œstrin effect and helps to produce a progestational reaction in the endometrium, thus tending to stop the bleeding.

### EFFECT OF FAILURE OF THE PITUITARY TO STIMULATE THE OVARY, OR OF PRIMARY OVARIAN FAILURE (FIG. 5)

When the ovary fails to secrete sufficient œstrin or progestin to stimulate the uterus the endometrium becomes atrophic and the uterus itself fails to grow,

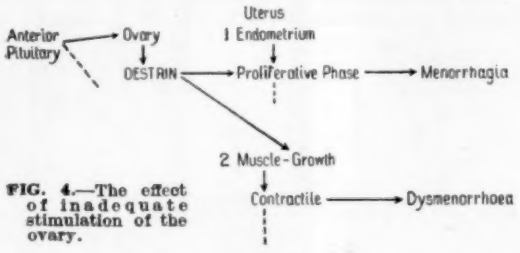


**FIG. 4.**—The effect of inadequate stimulation of the ovary.

remaining infantile in type and sometimes no larger than the tip of the little finger. This condition is associated with scanty and infrequent menses usually accompanied by dysmenorrhœa, or complete amenorrhœa, depending on the degree of ovarian failure. It is, of course, the cause of one type of functional sterility. It is found in most of these cases that artificial stimulation of the ovary by the administration of anterior pituitary extracts is insufficient to produce regeneration of the uterus. Large doses of œstrin are, however, sometimes successful in increasing the size of the uterus to adult proportions, and if they are followed by progestin the progestational phase will be induced with the subsequent onset of menstrual bleeding.

### INDICATIONS FOR THE USE OF PROGESTIN

A consideration of these inter-relations of the pituitary, ovary, and uterus provides a logical basis for the use of progestin in the following conditions.

1. *Habitual abortion.* (Premature withdrawal of progestin.)—Less than 30 rabbit units * is probably insufficient. We now advise the injection of 1 rabbit unit daily for two months, commencing a month before the usual time of abortion.

2. *Threatened abortion.* (Undue uterine motility.)—Steps should be taken to determine, as far as possible, whether the fœtus is still alive. One rabbit unit of progestin should then be administered daily until the signs of threatened abortion—i.e., bleeding and pain—have disappeared. The patient should, of course, remain at rest in bed during the treatment. It is obvious that a large series of cases is necessary before an opinion can be formed as to the value of progestin in this condition, for a number of apparent failures will be due to the fact that the fœtus was dead before the treatment was commenced. Moreover, an Aschheim-Zondek or Friedman test is not of much value in settling this point, for these tests often remain positive for as long as a month after death of

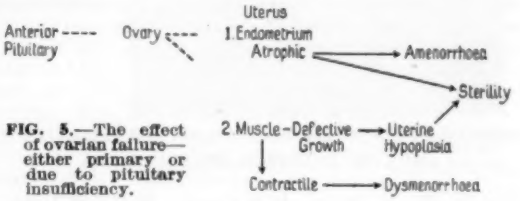


**FIG. 5.**—The effect of ovarian failure—either primary or due to pituitary insufficiency.

the fœtus. On the other hand, in a large number of cases of threatened abortion the symptoms disappear spontaneously and the pregnancy subsequently progresses normally.

3. *Functional Menorrhagia.* (Failure of ovulation and absence of progestin.)—In this condition progestin should be given in combination with anterior pituitary extracts. The anterior pituitary factor should be administered continuously by injections of up to 500 rat units three times a week in a course of two months' duration. The course may be repeated after a month or two's interval. In the premenstrual phase and during the actual time of the bleeding the anterior pituitary extract should be given daily, together with 1 rabbit unit of progestin.

4. *Dysmenorrhœa.* (Premature withdrawal of progestin.)—One rabbit unit should be given daily, commencing as soon as the pain appears, or a day or two before if possible, and continuing until the period ceases.

5. *Uterine hypoplasia; scanty, infrequent menses; amenorrhœa.* (Deficiency of œstrin and progestin.)—The result of treatment in these cases can best be evaluated by measuring the length of the uterus with a sound. This should, of course, be first undertaken before the treatment is commenced. The course of treatment is as follows: 250,000 international units of œstrin (in the form of di-hydro-œstrin benzoate) are administered by injection on the 1st, the 4th, the 8th, the 11th, and the 15th days of the course, giving a total of 2½ million units. On the 19th, 20th, 21st, 22nd, and 23rd days 1 rabbit unit of progestin is administered. Menstrual bleeding commences on

* One rabbit unit of progestin is equivalent to three clinical units. It is made up in oily solution, and is administered intramuscularly.

any day up to ten days after the last injection of progestin. This course, which was originally outlined by Kaufmann and is usually referred to as the Kaufmann technique, should be repeated once, and about a fortnight later the length of the uterus should again be measured. It is usually found to be increased and may have reached normal adult proportions as the result of the treatment, except in very severe and long-standing cases of secondary amenorrhœa, and in most cases of primary amenorrhœa, where the treatment does not appear to be effective.

Though we have been concerned, in this paper, solely with the endocrine causes of these cases of functional disorders of menstruation and pregnancy, other predisposing factors should not be neglected in treating these patients. The three most important considerations are the necessity for excluding organic lesions of the pelvic organs, the difficulty of obtaining an accurate and reasonable history and of assessing mainly subjective symptoms, and the difficulty of determining the degree of psychological disturbance.

Our thanks are due to Organon Laboratories, who have supplied us with most of the material, and to the Medical Research Council, on whose authority the original supplies were granted. Messrs. Schering also kindly supplied us with some Proluton which was used in one or two of the early cases.

## RENAL DWARFISM

### ASSOCIATED WITH VALVULAR OBSTRUCTION OF THE POSTERIOR URETHRA

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The occurrence of dwarfism, late rickets, and infantilism as sequelæ of chronic nephritis in childhood has been recognised since the appearance of the case reports of Morley Fletcher [1] in 1911, and subsequently those of Barber [2] and others. It is only recently, however, that attention has been particularly directed to the importance and frequence of other abnormalities of the urinary tract in cases of renal dwarfism. Prof. Arthur Ellis and Dr. H. Evans [3] have pointed out that dilatations of the bladder or ureters, or evidence of pyelitis, have been found in a considerable number of the published cases, and they add a report of 20 cases from the London Hospital, in 17 of which the urinary tract was specially investigated. In 14 of these there was evidence of dilatation of the bladder or ureters. Since no organic obstruction was found in the urethra in 14 cases on which post-mortem examination was carried out, the authors suggest a disorder of the neuromuscular mechanism controlling the urethro-vesical sphincter as the responsible factor. The present case is reported since it confirms Ellis and Evans's findings with regard to dilatation of the ureters and hypertrophy of the bladder, but differs from their cases in that an organic obstruction—namely, a valve—was found in the posterior urethra to account for the back pressure.

#### CASE REPORT

A. B., a male, was well until 3 years of age (May, 1927), when he was admitted to a fever hospital with diphtheria, and a diagnosis of nephritis was made on account of persistent albuminuria, thirst, and polyuria. On return home six months later he appeared pale and drowsy; the thirst and polyuria continued. He was brought to the Hospital for Sick Children, Great Ormond-street, at the age of 4 years 10 months, on account of genu valgum deformity of relatively rapid onset, and failure to grow. At this time he weighed 29 lb. (normal 40 lb.); the urine was of low specific gravity (1003) and contained no albumin on the first two examinations, though subsequently a trace or cloud has been present on each attendance. The blood-urea was 112 mg. per 100 c.cm.

After this he remained in moderately good general health, and was lively and cheerful, until the age of 8½ years (October, 1932), when he was admitted to hospital with five days' history of drowsiness, headache, and twitching. The blood-urea at this time was 238 mg. His weight was 32 lb. (normal 56 lb.). There was a considerable degree of anæmia, a blood count showing red cells, 2,800,000 per c.mm.; white cells, 15,000 per c.mm.; hæmoglobin, 35 per cent.; colour-index, 0·6; polymorphs, 63 per cent.; lymphocytes, 31 per cent.; large mononuclears, 4 per cent.; eosinophils, 2 per cent. He showed advanced rachitic deformities of knees, ankles, and wrists, with beading of the ribs and bossing of the skull. The blood pressure was 114/70, and there was clinically no enlargement of the heart. He passed between 600 and 1200 c.cm. urine a day, which contained a heavy cloud of albumin. There was no dysuria or retention, though there was nocturnal and diurnal frequency. The uræmic symptoms rapidly passed off in hospital, and he was discharged home. The rachitic deformities had by now become so severe as to prevent his walking, but he was able to ride a tricycle.

He was readmitted to hospital in January, 1933; intravenous pyelography was attempted, but was unsuccessful owing to delayed excretion. Cystoscopy was not thought advisable owing to the general condition. From this time his condition remained unchanged until he was readmitted in March, 1934 (aged 9 years 10 months), with œdema of face and dyspnœa. Fig. 1 shows his general appearance at this time. Weight 38 lb. (normal 65 lb.); height 40 in. (normal 52 in.). There was puffiness of the face but no œdema of the extremities. The mucous membranes were pale and the skin showed muddy discoloration. The fundi showed no changes except very marked retinal pigmentation. The blood pressure had risen to 130/95 (three weeks previously the systolic blood pressure had been 110). Whilst in hospital the boy suffered from frequency and urgency, with occasional dribbling incontinence of urine. The dyspnœa became more severe and he developed signs of ascites, death occurring after he had been six days in hospital. He remained mentally alert and cheerful to within a few hours of death.

The accompanying Table shows the results of biochemical investigations made by Dr. W. W. Payne.

| Date. | Blood-urea. | Non-protein nitrogen. | Serum calcium. | Plasma phosphorus. | (*a*) Blood cholesterol. (*b*) Plasma chlorides. | Plasma phosphatase (units). (Normal 5 to 15 units.) |
|---|---|---|---|---|---|---|
| Apr. 15, 1929 | 119 | — | 7·8 | 4·7 | (*a*) 202 | — |
| Sept. 16, ,, | 112 | 78·4 | 8·4 | 5·4 | — | — |
| Mar. 14, 1930 | 95 | 88 | 10·4 | 6·1 | — | — |
| ,, 20, ,, | 182 | — | 9·0 | 5·7 | — | — |
| Aug. 18, 1931 | 147 | — | 9·8 | 5·7 | — | — |
| May 2, 1932 | 182 | 112 | 8·2 | 7·6 | — | — |
| Oct. 18, ,, | 238 | — | 6·2 | 7·3 | — | 22·1 |
| Nov. 25, ,, | 244 | — | 6·7 | 7·2 | — | 62 |
| Jan. 26, 1933 | 129 | — | — | — | — | — |
| Mar. 21, 1934 | 225 | 185 | 3·84 | 10·4 | (*a*) 241<br>(*b*) 580 | 24 |

Values in mg. per 100 c.cm. except plasma phosphatase.

#### SUMMARY OF POST-MORTEM FINDINGS

Skin very pale, with muddy discoloration and numerous small pigmented patches on face. Skeletal deformities as above. Skull generally thickened, but cut abnormally easily. Brain œdematous. Heart showed moderate degree of enlargement, principally to left, measuring 9·5 cm. from right border to apex and weighing 185 g. The right ventricle was slightly dilated, and the myocardium soft and pale. The left ventricle was hypertrophied but not dilated, the wall measuring 1·5 cm. in thickness.

Valves normal. Aorta, radial and tibial arteries showed no abnormality. Peritoneal cavity contained 1000 c.cm. of clear yellow fluid, which on analysis showed 4·99 mg. calcium, 39·6 mg. inorganic phosphorus, 46·6 units phosphatase, and 366 mg. urea per 100 c.cm.; albumin, 2·95 per cent.; globulin, 1·47 per cent.; no fibrin present. Liver showed fatty changes. Spleen and gastro-intestinal tract normal. Thymus (9 g.), thyroid (10 g.), pituitary and adrenal glands appeared within the limits of normal.

*Genito-urinary tract* (Fig. 2).—Both kidneys were very small, the right measuring 5 cm. in length by 2·5 cm. in width, the left 6 cm. by 2·5 cm.; they weighed 10 and 11 g. respectively. The capsules were adherent, and the surfaces dark red and granular. There was no true hydronephrosis, but the pelvis of the left kidney was slightly dilated and that of the right kidney measured 2 by 2 cm. The left ureter was tortuous and dilated throughout its length, measuring 1·5 cm. in diameter immediately above the bladder. The right ureter was slightly dilated, particularly in the lower third. Both ureteric orifices admitted a medium probe. The bladder wall was greatly hypertrophied; mucosa not abnormal. A probe passed freely from the meatus into the bladder, but on opening the urethra from above a transverse fold of membrane was seen lying attached to the floor and walls of the urethra immediately below the openings of the ejaculatory ducts (Fig. 3). The verumontanum was prominent, with the mucosa thrown into fine radiating folds around it, and the prostatic urethra was dilated above the site of the valve. Below this the urethra appeared normal.

Microscopically the kidney showed great reduction in the number of glomeruli which were in all stages of degeneration. Those that remained were in some instances considerably hypertrophied, one measuring 408 μ (three to four times the normal) (Fig. 4). The tubules were widely separated by interstitial tissue, and many of them enormously dilated, containing fibrinous casts and red blood-cells. There was great increase in fibrous tissue throughout the section, particularly around the vessels and the pelvis. The interstitial tissue was infiltrated with very many small lymphocytes, and occasional eosinophils, plasma cells, and polymorphs. Scattered islets of regenerating tubules were seen.

FIG. 1.—The patient at the age of 9 years and 10 months, showing rachitic deformities and dwarfism; on the right a normal control of same age.

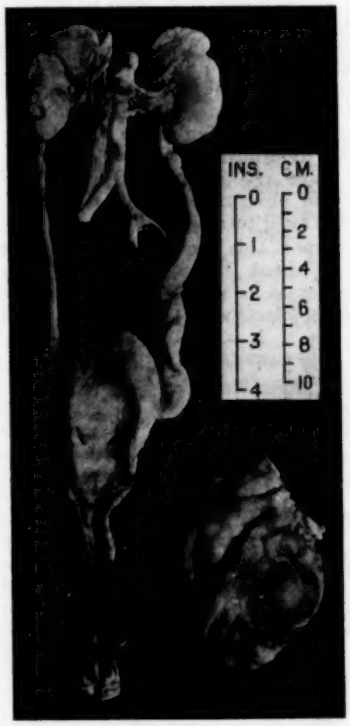


FIG. 2.—Atrophic kidneys (with adrenals attached), dilated ureters, and hypertrophied bladder; urethra opened from above to show position of valve (marked with an arrow). Heart showing moderate hypertrophy of left ventricle.

FIG. 3.—Drawing of valve in posterior urethra, situated immediately below orifices of ejaculatory ducts. The transverse fold of membrane was attached to the walls and floor of the urethra. Dilatation of prostatic urethra above valve; verumontanum prominent; bristles inserted into ureteric orifices.

DISCUSSION

The case presents features of both clinical and pathological interest, since not only was there little in the early history to suggest urethral obstruction, but also the question naturally arises as to whether the condition of chronic nephritis can be regarded as directly due to chronic back pressure. Hinman and Kutzman,[4] who collected 50 reported examples of congenital valvular obstruction of the posterior urethra, found that frequently characteristic symptoms, such as dribbling, incontinence, and dysuria, did not become obvious until infection of the dilated urinary tract had taken place. In this case, where there was no evidence of infection either clinically or post mortem, the symptoms of obstruction were effectually masked by those of chronic nephritis, frequency, and prolonged micturition (which may well have been due in part to a small stream) being attributed to polyuria. It was only as a terminal event that dribbling, incontinence, and urgency were complained of. The valve itself, which lay across the floor, and was attached to only half the circumference, of the urethra, would clearly cause only a partial obstruction, and was never sufficient to result in complete retention or great distension of the bladder. As in many of the recorded cases, it presented no obstruction to a probe passed in the opposite direction to the flow of urine. Morphologically, it corresponds to an incomplete variety of the third or "iris"

type of valve described by Young, Fronts, and Baldwin,[5] and from its position probably represents a remnant of the urogenital membrane (Bazy [6]).

Other points of clinical significance are the relative absence of hypertension until shortly before death (although some degree of cardiac hypertrophy had taken place), the long course after the blood-urea was known to be considerably raised, and the severity of the rickets in relation to the biochemical findings. The frequent absence of hypertension in this type of chronic nephritis in childhood was commented on by Ellis and Evans, who consider it characteristic only of the type of chronic nephritis associated with dilatation of the urinary tract. The long duration of the disease is also more typical of chronic nephritis in childhood than in adult life. In this instance the

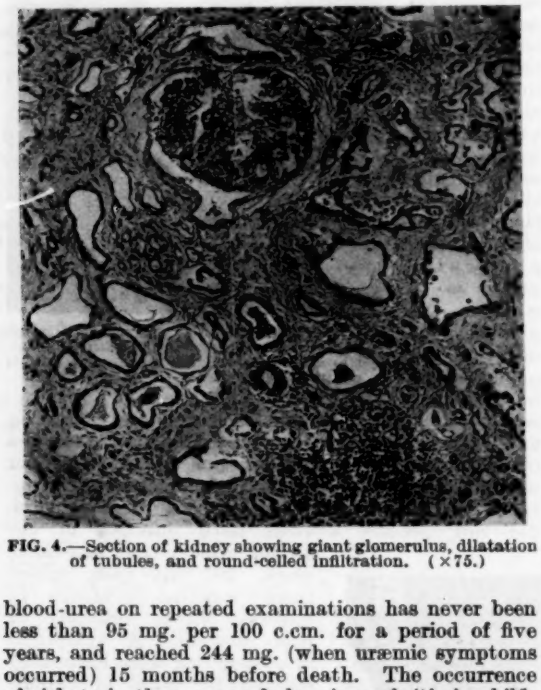

FIG. 4.—Section of kidney showing giant glomerulus, dilatation of tubules, and round-celled infiltration. (×75.)

blood-urea on repeated examinations has never been less than 95 mg. per 100 c.cm. for a period of five years, and reached 244 mg. (when uræmic symptoms occurred) 15 months before death. The occurrence of rickets in the course of chronic nephritis in childhood has been attributed by Parsons [7] to interference with the metabolism of calcium by the accumulation of phosphorus in the blood, this in turn being due to defective excretion of phosphorus by the kidney. Whilst there was in this case a definite tendency for the serum calcium to fall and the plasma inorganic phosphorus to rise as the disease progressed, bony deformities were actually occurring when the child first came under observation, and at this time the phosphorus value was only 4·7 mg. per 100 c.cm. Graham and Morris [8] point out that although the urinary excretion of calcium and phosphorus is greatly reduced in this condition, the retention of both elements is actually considerably less than the normal, owing to the greatly increased excretion in the fæces. The fact that as low a calcium value as 3·84 mg. per 100 c.cm. was obtained shortly before death in the absence of tetany is possibly explained on Lathrop's [9] hypothesis that an acidosis prevents the ionisable calcium falling to an extent corresponding to the fall in total calcium. The phosphatase values, which rose remarkably during the earlier uræmic period, are consistent with a condition of active rickets.

The causal relationship between congenital obstruction of the genito-urinary tract and the type of chronic nephritis described above is by no means clear. It is quite conceivable that *both* conditions may be congenital. There is some evidence that congenital nephritis may occur,[10 11] and congenital hypoplasia of the kidneys is well recognised; 33 per cent. of cases of congenital renal hypoplasia show in addition some other abnormality of the genito-urinary tract (Beer and Hyman [12]). Any form of obstruction would naturally tend to increase an already existing renal deficiency.

If, on the other hand, back pressure results in a condition of chronic nephritis in previously normal kidneys, it would appear that those types of obstruction which are of slight degree are most likely to produce this result. Most of the recorded cases of valvular obstruction have shown evidence of hydro- or pyo-nephrosis rather than chronic nephritis, though in some instances nephritic changes have been present in the remaining renal tissue, and in one of Hinman and Kutzman's cases it was found post mortem that the left kidney was granular and atrophic, whilst the right was hydronephrotic.

Whichever is the sequence of events, it seems advisable that investigation of cases of chronic nephritis in childhood which are unassociated with hyperpiesia or a previous history of acute nephritis should include an examination of the posterior urethra if there is at any time pyuria or evidence of dilatation of the bladder or ureters. As pointed out by Poynton and Sheldon,[13] valvular obstruction of the posterior urethra is easily overlooked even at post-mortem examination, unless the bladder and urethra are then removed in continuity. During life there may be few if any symptoms to point to urinary obstruction except when secondary infection has occurred, and it should be remembered that valves will frequently present no obstruction to the passage of a catheter though impeding the flow of urine from the bladder. Unfortunately, if the patient does not come under observation until retardation of growth or rachitic deformities have occurred, the renal damage will have reached a stage in which removal of a source of obstruction could hardly do more than postpone a fatal termination.

For permission to report this case, which was under their care, I wish to thank Dr. Robert Hutchison and Dr. E. A. Cockayne (who also presented the case before the children's section of the Royal Society of Medicine [14 15]).

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# AN EXPERIMENT IN FIRST-CLASS PROTEIN

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*With an Introduction by*

Sir F. Gowland Hopkins, F.R.C.P. Lond., P.R.S.

## Introduction

Dr. Corry Mann has honoured me by his desire that I should comment upon the following description of a most interesting experiment.

That proteins in different foods vary in their nutritional or "biological" value is now generally accepted as a fact of practical importance. Hitherto, in respect to human nutrition at any rate, the chief emphasis has been laid on the relative inferiority of vegetable proteins as compared with those of animal origin; but Dr. Mann, as the result of careful observations on himself, has obtained evidence which suggests that there may be marked differences in value between such proteins as those of milk and meat respectively.

The nature of Dr. Mann's experiment and its results, fully described by him in the paper which follows, may in briefest fashion be thus summarised: Having proved upon himself the adequacy of a selected basal diet which contained inter alia a ration of milk and another of meat, he then omitted half of the former and found that the diet was then no longer equal to his needs. On the other hand, when, instead of the milk, meat containing almost the same amount of protein was removed from the diet, its adequacy was apparently maintained. He holds that the most likely explanation of these results is to be found in the superior nutritional value of the milk proteins.

If this be so the circumstance is certainly one of much importance, and of special interest just now, when so much effort is being spent to secure a safe national milk-supply and its proper distribution.

Experiments dealing with the biological values of proteins have been very numerous on animals, but few have been made on man. Prominent among the latter are those carried out upon himself by Karl Thomas in 1909. The method used by him measured the relative powers of various proteins to spare the body from a loss of tissue proteins. According to Thomas the biological value of meat proteins taking that of milk proteins as 100, is 104; that is to say, they are practically identical, the difference found being within the limits of experimental errors. Martin and Robison however when describing some very careful observations of their own, pointed out that the figures given by Thomas for milk were open to criticism. They agreed with him however in finding that wheat proteins have for the human body a much lower value than those of milk, but they did not compare the latter with other animal proteins. It would appear indeed that on human subjects no satisfactory comparisons have been made; Corry Mann's experiment on himself is so much the more welcome.

Certain aspects of the experiment and its results call for comment. I think it may be said first of all that Dr. Mann did well to study the effects of the varying diets while continuing his ordinary avocations. This enabled him to follow their effects during long periods under normal conditions. Experiments in the laboratory have generally involved the subject in the consumption of a protein-free diet for a few days and then, also for periods of a few days, of the same diet plus the protein or proteins under study until the amount of each which will restore nitrogenous equilibrium is determined. Less of a superior and more of an inferior protein will be required to accomplish this. Such results have a quantitative character, but the experimental periods have usually been too short and the conditions have often proved trying to the health of the subject, leading to unsatisfactory results.

Dr. Mann made the necessary effort involved in maintaining for long periods that standardisation of daily activities which is essential for such an experiment. Always assuming that the amount of protein eaten is not greatly in excess of current needs, there can be no better method of comparing one protein with another than that of simple replacement during the continuance of routine activities conscientiously maintained. The criteria available for the evaluation of the diets were, it is true, mainly based on subjective symptoms; for although the body-weight was recorded and shown to remain constant on the favourable diets, the loss was small even on the least favourable. No determinations were made of the nitrogen balance of the body. Dr. Mann however is a trained observer, and we may be sure that the subjective symptoms were accurately noted and evaluated.

In considering the results attention must be given to the possibility that the favourable influence of the milk ration was due to factors other than a superiority in its proteins. Any suggestion that the milk proteins are easier of digestion than those of meat can, I consider, be ignored. There is available evidence to show that the difference is very small and inconstant. It might be urged that when milk is removed from a dietary there will be a greater loss of vitamins A and D than when meat of equal protein content is removed, and that this might account for, or contribute to, the superiority of milk over meat. I think however that after the removal of either, the residue of Dr. Mann's basal dietary contained sufficient of these vitamins for the adult body, while the symptoms he describes as following the use of the unfavourable diet do not seem to have been those of vitamin deficiency.

One aspect of the results may seem puzzling. In his classical experiments at Woodford which have established Dr. Mann's high reputation as a student of nutrition, he himself found that the addition of casein to the institutional diet of boys produced much less extra gain in weight and growth than did a milk ration containing approximately the same amount of protein. It would seem therefore at first sight that factors other than superiority in its proteins must have accounted for the highly favourable influence of milk in the Woodford experiment. Doubtless this was in part the case, for the basal diet there was deficient in animal fats, while margarine replaced butter. It is likely therefore that vitamins A and D were deficient and while the milk ration increased them the casein ration of course did not. Nevertheless the Woodford results with casein do not make negative other evidence for the superiority of milk proteins over meat proteins, and as bearing on the present experiment it should be remembered that the mixed proteins in milk yield together a more favourable amino-acid balance than is found in casein itself when isolated from its associates.

It is a circumstance worthy of notice that the subject of this experiment, when on the basal diet from which meat was withdrawn, maintained his

health, and activities, which though not strenuous were equal to those of a large section of the public, while consuming some 60 g. of protein of which only 42 g. were of the so-called first-class variety. It may be asked whether this is because so much of the latter was composed of milk proteins. It should be noticed further that this apparently adequate diet contained little more than 2000 calories.

In conclusion I would like to express the opinion that Dr. Corry Mann's experiment on himself should direct attention to what may well be a very important point in practical dietetics. All will agree, however, that a final proof of the superiority of milk proteins for human nutrition must ultimately be based upon a fully controlled experiment on numerous individuals, and best on young individuals, such as that carried out so admirably at Woodford by Dr. Corry Mann on behalf of the Medical Research Council. It is much to be wished that he who conducted that investigation might be given the opportunity of extending it in circumstances equally favourable.

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## The Observations

This experiment was planned with the idea of setting a value to the minimum requirements of first-class protein for an adult, with a secondary aim of comparing the protein of milk with that of another common item of an ordinary diet.

Anyone who has undertaken research in experimental dietetics will realise that in an investigation of this sort the first consideration is to schedule a "basic diet" which suits the particular occupation of the person who forms the subject of the test and also that person's basic metabolism. The basic diet so chosen must maintain the nutrition of the individual without deterioration in health, and at the same time allow him to carry out his daily occupations whether in pursuit of a livelihood or in satisfaction of recreational activities. Such a diet will vary much, both in calorie value and in composition, with different persons. The basic diet here detailed had been tested at intervals, for varying periods, during ten years and it had been found to be adequate between the years 1921 and 1931.

The subject of experiment was a man of middle age. His weight was 145 lb. with a constant summer-to-winter and winter-to-summer swing. His medical history for some 30 years, even under active service conditions, had been singularly uninteresting from a doctor's standpoint. His occupation—partly sedentary—was of a routine nature for about half of each week. During the remainder of the week his work was of a more varied type and involved travelling by car or train but with little expenditure of muscular effort. With the start of the experiment in 1931 a definite amount of walking exercise was introduced. Certain distances were plotted out on the map and time-distance was logged weekly, any excess or deficiency of exercise during one week being immediately corrected in the following week. In this way an average of 15 miles timed walking exercise was maintained, while the experiment was in progress, during each week.

### THE EXPERIMENT DESCRIBED

1. The basic diet was taken, with the additional scheduled weekly exercise, for a period of four months (Diet No. 1). Result: similar to previous experience. General health remained normal with body-weight showing a normal daily swing.

*Diet, experimental.* Kensington, 1931, 1932, 1933. Weight 145 lb.

| | | | Grammes in ration. | | |
|---|---|---|---|---|---|
| *8.15 a.m.* | oz. | Calories. | Protein. | Fat. | Carbohyd. |
| Orange | 3·5 | 40 | 0·80 | 0·11 | 8·80 |
| Toast | 3·5 | 233 | 7·00 | 0·70 | 48·30 |
| Butter | 1·0 | 221 | — | 23·86 | — |
| 2 eggs | 3·0 | 138 | 10·46 | 9·56 | 1·38 |
| Marmalade | 1·0 | 80 | 0·04 | — | 19·48 |
| Tea | — | — | — | — | — |
| Milk (*a*) | 7·0 | 133 | 6·58 | 7·28 | 9·52 |
| Total g. | — | — | 24·88 | 41·50 | 87·48 |
| Total calories * | — | 846 | 102 | 386 | 358 |
| Per cent.: calories | — | — | 12 % | 45 % | 42 % |

| *1.30 p.m.* | oz. | Calories. | Protein. | Fat. | Carbohyd. |
|---|---|---|---|---|---|
| Cheese | 1·0 | 146 | 7·50 | 12·22 | 0·71 |
| Salad | 2·0 | 8 | 0·62 | 0·11 | 1·08 |
| 3 creamcrackers | 1·0 | 122 | 3·60 | 1·50 | 22·80 |
| Butter | 0·5 | 110 | — | 11·93 | — |
| Baked apple (*b*) | 3·5 | 43 | 0·30 | 0·20 | 9·80 |
| Rice pudding (*c*) | 4·0 | 153 | 3·74 | 7·47 | 16·88 |
| Milk (*a*) | 3·0 | 57 | 2·79 | 3·06 | 4·26 |
| Total g. | — | — | 18·55 | 36·49 | 55·53 |
| Total calories * | | 642 | 76 | 339 | 227 |
| Per cent.: calories | — | — | 11 % | 52 % | 35 % |

| *4.30 p.m.* | oz. | Calories. | Protein. | Fat. | Carbohyd. |
|---|---|---|---|---|---|
| Bread | 1·0 | 66 | 1·98 | 0·19 | 13·72 |
| Butter | 0·25 | 55 | — | 5·96 | — |
| Jam | 0·5 | 41 | 0·02 | — | 10·14 |
| Cake (*d*) | 1·0 | 98 | 2·00 | 3·49 | 14·02 |
| Tea | — | — | — | — | — |
| Milk (*a*) | 7·0 | 133 | 6·58 | 7·28 | 9·52 |
| Total g. | — | — | 10·58 | 16·92 | 47·40 |
| Total calories * | | 394 | 43 | 157 | 194 |
| Per cent.: calories | — | — | 10 % | 39 % | 49 % |

| | | | Grammes in ration. | | |
|---|---|---|---|---|---|
| *7.45 p.m.* | oz. | Calories. | Protein. | Fat. | Carbohyd. |
| Clear soup | 8·0 | 4 | 1·00 | — | — |
| Mutton cutlet (*e*) | 2·0 | 96 | 11·08 | 5·44 | — |
| Tomato | 3·0 | 19 | 0·59 | 0·08 | 3·83 |
| Spinach (*f*) | 1·0 | 6 | 0·51 | 0·05 | 0·84 |
| Toast | 1·0 | 66 | 1·98 | 0·19 | 13·72 |
| Orange | 3·5 | 40 | 0·80 | 0·10 | 8·80 |
| Coffee (or tea) | — | — | — | — | — |
| Milk (*a*) | 4·0 | 76 | 3·76 | 4·16 | 5·44 |
| Total g. | — | — | 19·72 | 10·02 | 32·63 |
| Total calories * | | 307 | 81 | 93 | 133 |
| Per cent.: calories | — | — | 26 % | 30 % | 43 % |

* by calculation.

SUMMARY

| | | Grammes. | | |
|---|---|---|---|---|
| | Calories. | Protein. | Fat. | Carbohyd. |
| 8.15 A.M. | 846 | 24·88 | 41·50 | 87·48 |
| 1.30 P.M. | 642 | 18·55 | 36·49 | 55·53 |
| 4.30 P.M. | 394 | 10·58 | 16·92 | 47·40 |
| 7.45 P.M. | 307 | 19·72 | 10·02 | 32·63 |
| Total g. | — | 73·73 | 104·93 | 223·04 |
| Total calories † | 2191 | 302 | 975 | 914 |
| Per cent.: calories | | 13 % | 44 % | 41 % |

† by calculation

↓

or 15·1 calories per lb. of body-weight at 145 lb.

Total animal protein .. .. 52·88 g. (70 % total protein)
Total animal fat .. .. 98·19 g. (93 % total fat)

*Note.*—There is also a small quantity of milk in the biscuits and of butter in the cake.

(*a*) Pasteurised milk. Daily total 21 oz.
(*b*) Or other stewed or fresh fruit in equivalent calories.
(*c*) Rice pudding made from:—

| | oz. | Calories. | Protein. | Fat. | Carbohyd. |
|---|---|---|---|---|---|
| Rice | 1·0 | 102 | 1·84 | 0·10 | 22·90 g. |
| Milk | 10·0 | 190 | 9·40 | 10·40 | 13·60 g. |
| Butter | 0·5 | 110 | — | 11·93 | — |
| Sugar | 0·5 | 58 | — | — | 14·16 g. |
| Total | 12·0 | 460 | 11·24 | 22·43 | 50·66 g. |
| Ration | 4·0 | 153 | 3·74 | 7·47 | 16·88 |

(The ration contains 3·3 oz. milk with 3·13 g. milk protein. 7·44 g. milk fat.)

(*d*) Contains butter.
(*e*) Or mutton chop or minced mutton.
(*f*) Or cabbage, or lettuce.

2. Ten ounces of milk were deducted from the diet, taking 3 oz. from each of the first two meals and 4 oz. from the 4.30 P.M. meal. This may be called Diet No. 2.

The new values may be tabled thus :—

| | Calories. | Grammes in rations. Protein. | Fat. | Carbohyd. |
|---|---|---|---|---|
| Basic Diet No. 1 .. | 2191 .. | 73·73 .. | 104·93 .. | 223·04 |
| Milk, 10 oz. deducted | 191 .. | 9·40 .. | 10·40 .. | 13·60 |
| Diet No. 2 .. .. | 2000 .. | 64·33 .. | 94·53 .. | 209·44 |

*Note.*—The animal protein is thus reduced from 52·88 to 43·48 g.

This diet was given in all for six weeks. During the first five weeks there was a slow steady fall in weight, with a general deterioration in physical condition. The subject of experiment, who was quite accustomed to spend a busy day without fatigue, found that after a morning's routine he became unusually tired by 1.30 P.M. These symptoms of deterioration becoming more troublesome in the sixth week the Diet No. 2 was discontinued.

3. The basic diet—No. 1—was resumed and continued for three months. During the second week there was a definite improvement in physical condition and normal health was rapidly regained.

4. Diet No. 3 was then substituted for the basic Diet No. 1. The items deducted to form Diet No. 3 were selected to give a value equivalent in calories to the milk deducted to form Diet No. 2, and containing about the same amount of animal protein and animal fat. The new values may be tabled thus :—

*Deductions :*

| | oz. | Calories. | Grammes in rations. Protein. | Fat. | Carbohyd. |
|---|---|---|---|---|---|
| Mutton (7.45 P.M.) | 2·0 .. | 96 .. | 11·08 .. | 5·44 .. | — |
| Cake (4.30 P.M.) .. | 1·0 .. | 98 .. | 2·00 .. | 3·49 .. | 14·02 |
| Total deductions | | .. 194 .. | 13·08 .. | 8·93 .. | 14·02 |

*and therefore :*

| | | | | | |
|---|---|---|---|---|---|
| Basic Diet No. 1 | — | ..2191 .. | 73·73 | ..104·93 .. | 223·04 |
| Deductions as above | | .. 194 .. | 13·08 | .. 8·93 .. | 14·02 |
| Diet No. 3 .. | — | ..1997 .. | 60·65 | .. 96·00 .. | 209·02 |

*Note.*—The animal protein is thus reduced from 52·88 to 41·80 g.

This diet was given for several weeks. The subject of experiment remained fit without unusual fatigue, the physical condition remained good and the diet satisfied.

5. It was decided to repeat the experiment with Diet No. 2, in order to exclude neurosis. For this purpose the basic Diet No. 1 was again resumed and was maintained for three months, the general health remaining normal with a steady body-weight at the average level.

6. Diet No. 2 was resumed (vide supra). On this occasion 10 oz. of hot water were taken every night in order to exclude any possibility that the symptoms of physical deterioration, which had been previously experienced, were due to diminution of fluid intake. Result: physical deterioration, after four weeks, was again obvious. The diet—No. 2—was maintained for a full six weeks with symptoms of lassitude increasing and a total fall in weight of 2·25 lb.

7. Return to basic Diet No. 1. Slow progress for a fortnight, followed by steady recovery.

### SUMMARY

It would seem therefore that, for the individual in question, the presence of a full ration of 21 oz. of milk in the diet described, which contained a small additional quantity of boiled milk in a helping of milk-pudding, enabled general health to be maintained without deterioration, even when the total protein had been reduced to 60·65 g. daily and the total animal protein to 41·80 g. daily (Diet No. 3). On the other hand, a reduction of total protein to 64·33 g. and of animal protein to 43·48 g. was followed by progressive deterioration in physical condition if only 11 oz. of milk remained in the diet in addition to the small quantity of boiled milk above mentioned. In other words, the protein of milk appears to be of more value for purposes of nutrition than the protein of meat.

### FURTHER NOTE

Attention is drawn to the fact that the most important meal in this schedule is the breakfast, and it is suggested, not only from these observations but from others which have been made with diets employed during conditions of most strenuous physical exertion, that fatigue in industry would be less marked if employers of labour could offer facilities for a breakfast which is something more than a hasty and insufficient meal. Such a breakfast would contain well-balanced rations including first-class protein, adequate fat, and vitamins, without undue loading with carbohydrate, having regard to the fact that carbohydrate alone—even as dextrose—is insufficient to prevent the after-effects of fatigue. There are also the considerations of climate in this country, which for the greater part of the year is colder and more moist—more productive of rheumatic infections—than the climate of those more southerly European countries where an English breakfast is considered unnecessary.

Lastly, I would lay stress upon the fact that the milk which was used for the purpose of the experiment was milk which had been pasteurised by the low-temperature process—a process which implies adequate thermostatic control. The milk was a daily sample of the milk-supply in Kensington from the local pasteurisation plant. The source of the milk was not selected for the experiment, nor had the firm supplying the milk any knowledge at all of the test.

I know of no evidence in support of the contention that the nutritive value of milk, as a whole, or of its vitamins or of its protein, is damaged by pasteurisation to an appreciable degree. Experimental work in human nutrition is against such a claim. Many of the wild statements, which have been made, that irreparable damage is done to the nutritive value of milk by the process of pasteurisation are prompted by an ulterior motive—to lower the charges of milk distribution. No milk is really safe that has not been pasteurised. The best milk is that which comes from a tuberculin-tested herd and which is subsequently pasteurised by the low-temperature process.

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## TRANSITORY REDUPLICATION OF THE SECOND TRICUSPID SOUND AS A SOLE SIGN OF CORONARY THROMBOSIS

By J. H. Williams, M.B., B.Sc. Wales

THE patient is a well-built, very healthy looking man of 54. He is a caretaker at a large institution, where his work is not heavy, consisting mainly of attending to furnace fires and the lawns and gardens.

Before he came under my care in 1928 he had been told that his blood pressure was higher than normal, and so he used to come to see me periodically to have it checked. He did not complain of any ill-health, and there was no evidence of any organic disease. The blood pressure was usually 150/90 when he came to see me, though once or twice I found it as high as 160/90. On these occasions a short period of treatment by the administration of potassium iodide brought it down to 140/90, though it had a tendency to rise again slowly.

He usually knew when it had gone up, as he then experienced vague pains in the chest, with palpitation, and occasionally slight pains down the left arm. These symptoms were not related to exercise. Previous to the present illness he last came to see me in December, 1931, when the blood pressure was 130/90.

On the evening of Oct. 8th, 1933, he was sitting at home with his family. He stooped to pick up some article which he had dropped, and as he got up he "fainted," a thing which he had never done before. He fell back

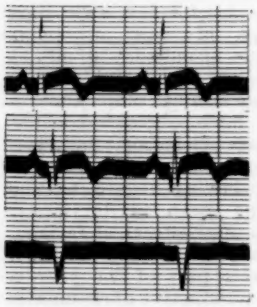

FIG. 1 (Nov. 2nd, 1933).

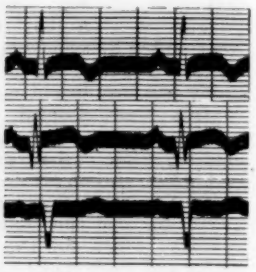

FIG. 2 (Nov. 9th).

in his chair, became deathly pale, and groaned continually. His head rolled from side to side, but there were no twitchings of the upper limbs. The attack lasted for five or seven minutes, and soon after he had recovered he felt fairly well, though rather shaken. He did not complain of having experienced any pain during the attack. He came to see me the next evening and told me of his "fainting attack." It was difficult to realise that there could be anything the matter with him. A well-built, alert, fresh-complexioned man, he looked the embodiment of perfect health.

On examination the pulse was regular in force and rhythm. The heart was a very little enlarged towards the left and the sounds were rather faint, but this was thought to be due to the well-developed chest wall. No murmurs were heard. The blood pressure was 150/90. He said that he felt perfectly well, but I had an idea that he did not really feel as well as he said he did. He looked rather apprehensive and just the least bit frightened.

Although there were no abnormal physical signs to be made out by the ordinary methods of examination, I was suspicious that he might have had an attack of coronary thrombosis; and, in view of his history of increased blood pressure and his uneasy manner, I advised him to go to bed and stay there for at least a fortnight. At first he refused unconditionally, but after some persuasion he went to bed and stayed there for nearly a fortnight. During this time I visited him frequently. The heart sounds became a little clearer and were quite pure, but nothing else different in the cardiac condition was noted. A Wassermann reaction was done and found to be negative.

On Oct. 23rd he looked and felt quite well, and said he felt no effects at all of the attack he had had 14 days before. It was then arranged that an electrocardiographic examination should be made on Oct. 26th, but on that day he sent for me and told me that he did not feel like going to be examined as he had had a slight cold a day or so before. Again he appeared to be apprehensive and ill at ease. On examination he appeared to have no signs of a cold. The pulse was a little slower than usual—62 per minute. On auscultation of the heart the cardiac sounds were rather distant but quite clear, except for a very striking reduplication of the second tricuspid sound. This was quite clear and in marked contrast to the sounds in the other parts of the precordium. No murmurs were made out. He remained in bed for some days more, and was eventually electrocardiographed on Nov. 2nd by Dr. William Phillips of the Medical Unit of the Welsh National School of Medicine, Cardiff. The reduplication of the second sound had by this time disappeared.

The electrocardiogram (Fig. 1) shows normal sinus rhythm with left axis deviation; there is an abnormally large Q in leads II. and III.; the S–T "take-off" is above the iso-electric level in leads I. and II., and in these leads a negative T wave is preceded by a high convexity of the S–T interval. These findings are typical of a recent coronary occlusion, but as Dr. Phillips had been unable to elicit any history suggestive of this, from either the patient or his wife, he was rather puzzled; and as he also had noticed their uneasy and apprehensive manner, he wrote to me with a view to obtaining, if possible, some history of a recent anginal attack. I therefore had a talk with the patient and, after putting a few leading questions, elicited the following information.

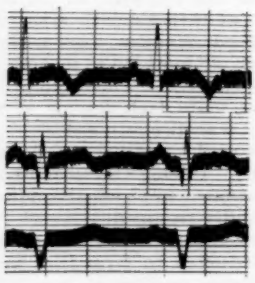

FIG. 3 (Nov. 23rd).

On the night of Oct. 24th he had a severe attack of pain over the lower half of the sternum. The pain was agonising and lasted nearly three hours. He did not faint, but his wife told me his colour was greyish-white, and that he looked as though he might die at any moment. She was too frightened to leave him to send for me; and being so frightened by the ominous gravity of the attack, they deliberately refrained from a true description of the attack, hoping to get some assurance from an objective examination of the heart. Later on he stated that for three or four months past he had experienced some tightness in the chest when walking uphill which forced him to stop and rest. When I examined him and noted the reduplication of the second tricuspid sound 36 hours had elapsed since the attack. Within four days it had disappeared.

After this examination the patient continued to rest for the greater part of the day, and was electro-

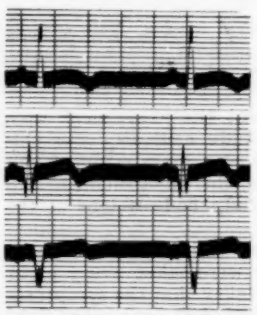

FIG. 4 (Jan. 4th, 1934).

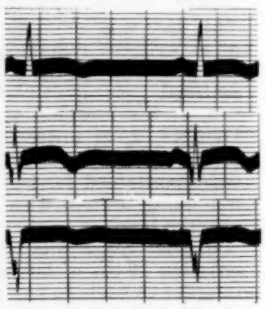

FIG. 5 (Feb. 1st).

cardiographed again on Nov. 9th, 1933, and again on the 23rd, and resumed light work on the 27th. He has remained well since, and further electrocardiograms were taken on Jan. 4th and Feb. 1st, 1934. These electrocardiograms (Figs. 2, 3, 4, and 5) show successive changes which confirm the original opinion that the findings were due to a recent coronary occlusion. The deep Q deflections in leads II. and III. persist; the "take-off" of the S–T interval returns to the iso-electric level in lead I. and almost to that level in lead II.; the T wave in leads I. and II. tends to become positive again; and the flat T of lead III. becomes mainly positive. It is not unusual to find Q changes in leads II. and III. when the T changes are in the main confined to leads I. and II. From these changes in the electrocardiogram alone there is very little doubt as to the diagnosis; with the history of the prolonged anginal attack the changes are diagnostic.

Until electrocardiographic evidence which pointed so certainly to coronary thrombosis had been obtained, the diagnosis in this case was not at all clear. The

history given by the patient and his wife after the anginal attack had been that of a cold, and not of an attack of agonising pain. He subsequently told the true story of the attack, and admitted that they had been so frightened by its severity that they had deliberately refrained from a full description.

Apart from the striking reduplication of the second tricuspid sound there was nothing which would suggest the advisability of a more detailed examination of the heart; and apart from the results of the electrocardiographic examination the patient might have been allowed to return to his ordinary work, without any special caution, well within the danger period of six to eight weeks after an attack of coronary thrombosis had taken place. It would seem, therefore, that this sign, appearing for a period of but a few days, is of considerable diagnostic significance.

In the literature there appears to be no reference to such a physical sign as a reduplication of the second tricuspid sound in an otherwise apparently normal heart. While in coronary artery disease and consequent cardiac failure it is not unusual to find reduplication of the second sound and various forms of gallop rhythm, especially in the cardiac failure following coronary occlusion, these are usually associated with the development of intraventricular or auriculo-ventricular block, or of failure more especially of the left ventricle; and in these cases the gravity of the heart lesion is at once apparent.

Two cases of coronary occlusion are, however, described by Wolferth, Wood, and Margolies,[1] where auscultatory signs confined to the tricuspid area were observed.

In each case the patient was obviously ill and was being carefully studied in hospital. In the first case from the fifteenth to the twenty-third day, and in the second case from the fifth to the twenty-seventh day after the closure a presystolic murmur was heard in the tricuspid area and recorded by phonocardiogram. The observers discuss the mechanism of this murmur, and conclude that "it seems to be produced by the flow of blood from the right auricle to the right ventricle," and to be "probably related to convalescence from acute coronary thrombosis." The explanations most favoured by the observers are "possibly because the structures near the tricuspid valve are œdematous; possibly because the interventricular septum is thin, and bulges into the right ventricle; possibly because in certain cases mural thrombi occur in the right ventricle in such a position as to interfere with the opening of the tricuspid valve."

They conclude that "the character of the murmur and its area of audibility are unusual enough to make its occurrence of possible diagnostic assistance in some cases."

Both these cases were considered to be instances of occlusion of the left anterior descending coronary artery, with infarction of the anterior surface of the left ventricle. This localisation was based on the electrocardiographic finding of the T 1 type of curve. This method of localisation is apparently accurate in at least the majority of cases, although more than one authority does not accept it.

I suggest that the reduplicated tricuspid second sound described in this note had an origin similar to that of the presystolic murmur noted in the article cited; and I feel that any patient showing a similar transitory sign should receive very careful electrocardiographic examination before being dismissed as healthy. It is quite reasonable to suppose that signs of this nature occur more frequently than would appear from the absence of references in the literature, and that they have not been reported previously because of this transitory nature; and that anticipation and observation of such a sign would lead to the more complete investigation and diagnosis of cases of "fainting" of obscure origin, which, owing to the patient's apprehension and concealment of facts, lead to a fatal termination in cases of so-called symptomless coronary thrombosis.

[1] Wolferth, C. C., Wood, F. C., and Margolies, A.: Amer. Jour. Med. Sci., 1933, clxxxvi., 496.

SUMMARY

A case of T 1 type of coronary thrombosis is recorded, in which a striking reduplication of the tricuspid second sound occurred for four days after the closure. This was the only sign of cardiac abnormality, as the history of the coronary attack was not obtained until after electrocardiographic diagnosis had been made, owing to the patient's apprehension.

As a result of this apprehension and the otherwise normal findings on examination of the heart, the patient might reasonably have been dismissed as having no abnormal condition and allowed to return to ordinary work, probably with disastrous results.

The view is put forward that a transitory reduplication of the tricuspid second sound is highly suggestive of coronary thrombosis, and that any patient showing this sign after a "fainting attack" should be submitted to expert electrocardiographic examination before being allowed to return to his usual duties.

I desire to express my thanks to Dr. Phillips for the electrocardiograms and for his valuable assistance in this case.

# Clinical and Laboratory Notes

## DESCENDING INFECTION OF THE URETHRA

BY MORTON WHITBY, M.R.C.S. Eng.

GENITO-URINARY SURGEON TO ST. MARGARET'S CLINIC FOR TUMOURS; CONSULTING UROLOGIST TO THE FINNISH SEAMEN'S MISSION

ACUTE non-gonorrhœal urethritis is uncommon—so uncommon indeed that urological books barely mention it. Nelson's "Index of Surgery" (Urological Section) gives the best account. It describes the condition as extremely rare, and adds: "In cases of pyelitis, pyelonephritis, pyonephrosis, etc., with cystitis, urethral inflammation is occasionally noted, but not as frequently as one would expect in view of the fact that the urethra is so frequently bathed with infected urine. Either the urethra is relatively immune from infection from this source, or the condition is overlooked and overshadowed by the more important condition in the upper urinary tract."

The two following cases illustrate the condition of infection descending from the upper urinary tract and causing urethritis, presumably by direct spread.

CASE 1.—A man aged 38, a sales manager, consulted me on July 2nd, 1934, complaining of a blood-stained urethral discharge which had come on suddenly a few days before. He complained of some initial difficulty of micturition which was overcome after the emission of a few blood clots. There had been increased diurnal frequency for some time. He had never passed a stone. His general health was good except for occasional indigestion and obstinate constipation. I found that the right kidney was palpably enlarged. The prostate was normal. The urethra emitted a small amount of sticky blood-stained purulent discharge. Microscopical examination of the discharge revealed an abundance of pus cells, epithelial cells, red cells, but no gonococci or other micro-organisms. The urine was acid and contained pus and albumin; culture was negative. Radiological examina-

tion revealed a small shadow in each kidney which moved with the kidney. Uroselectan demonstrated hydronephrosis on the right side, and cystoscopy showed hæmorrhagic cystitis, ureteritis, and trigonitis. The indigo-carmine test was normal.

The urethritis in this case was clearly due to bilateral renal calculi. These passed naturally, and the symptoms disappeared after treatment with bland fluids ad lib, urinary antiseptics, colonic irrigations, and bladder irrigations.

CASE 2.—The second patient, a man aged 35, an antique expert, consulted me on July 4th, 1934, complaining of a purulent blood-stained discharge which had come on suddenly after coitus with his wife a few days previously. He had had diurnal frequency of micturition for some time. He had never passed a stone. His general health was fair except for recent obstinate constipation. He had gonorrhœa in 1922, treated privately for three months. His father died of cancer of the bladder at the age of 54. Examination showed the kidney, prostate, and vesicles to be normal clinically. The urethra emitted a little blood-stained purulent discharge which microscopically contained pus, epithelial, and red cells, but there was no sign of gonococci or other micro-organisms. A prostatic smear was negative. The urine was acid and contained pus and albumin, oxalate crystals, *Bacillus coli*, and dead spermatozoa. Culture was negative. Uroselectan demonstrated early hydronephrosis on the right side with a suggested filling defect of a lower calyx. Cystoscopy showed the presence of cystitis, ureteritis, and trigonitis. The indigo-carmine test was slightly delayed on the right side.

Hydronephrosis infected with *B. coli* was the apparent cause of the urethritis in this case, and cleared up with the same treatment as the other case. In view of the family history and the suggested filling defect of a calyx, a further uroselectan or ascending pyelogram will be done shortly.

## AN EARLY CLINICAL SIGN OF ACUTE MASTOIDITIS

### THE RESERVOIR SIGN

BY N. ASHERSON, F.R.C.S. Eng.

ASSISTANT SURGEON, THE CENTRAL LONDON THROAT, NOSE AND EAR HOSPITAL; SURGEON FOR DISEASES OF THE EAR, NOSE AND THROAT, QUEEN'S HOSPITAL FOR CHILDREN

AN acute symptomless mastoiditis commonly manifests its presence by a persisting, profuse (usually, but not necessarily, pulsating) ear discharge, following on an attack of acute otitis media. This somewhat vague qualitative clinical observation may be expressed quantitatively—and thus made of definite diagnostic significance—by a consideration of the reservoir sign. This latter depends on the fact that secretions in the mastoid antrum and/or mastoid air-cells pour through the aditus and attic into the tympanic cavity before passing into the meatus, through a perforation in the tympanic membrane. If all the secretions are removed from the meatus, any rapid reaccumulation must arise from the mastoid, since secretions from the tympanic cavity alone take many hours to reform. The word secretion is taken to connote a mucoid, a muco-purulent, or a purulent discharge.

*The reservoir sign.*—All secretions are removed from the meatus by gently syringing, followed by mopping, or by mopping alone. The meatus is then examined (with the electric auriscope) to confirm that it is thoroughly dry, especially in the sinus of the meatus (the part where the tympanic membrane adjoins the floor of the meatus). The meatus is again examined at the end of 15 and at the end of 30 minutes. If the meatus remains dry the reservoir sign is negative; if, in the interval, secretions have reappeared in the depth of the meatus, the reservoir sign is positive.

The reaccumulation first fills the sinus of the meatus. If the reaccumulation is rapid, the entire tympanic membrane, previously dry and visible, is now obscured by the secretions. In a marked case, after the meatus has been cleared and the perforation in the tympanic membrane is exposed, beads of secretion may be observed to ooze out through the perforation (see case below).

A positive reservoir sign is often accompanied by pulsation, but the latter sign, per se, has little diagnostic significance.

If the sign is only doubtfully positive after 30 minutes the patient should be confined to bed for 24 hours, and the test should be repeated. This may convert a doubtfully positive into a definitely negative sign.

*Significance of the reservoir sign.*—The sign has no significance within the first 48 hours, after spontaneous perforation of the tympanic membrane, or after myringotomy, in a case of acute suppurative otitis. After the third day from perforation or myringotomy the presence of a positive reservoir sign is diagnostic of acute mastoiditis. When positive then it is the earliest clinical sign of acute mastoiditis, even when the only sign and symptom present. The tympanic membrane itself may show signs of resolution.

CASE 1.—A child of 5 complained of earache due to acute suppurative otitis media. The temperature was 101° F. The tympanic membrane was incised. At the end of 48 hours the only sign was slight fever, and the child was well. The reservoir sign was positive with pulsations in 20 minutes. Operation revealed extensive mastoid cellular involvement.

A negative reservoir sign does not exclude a diagnosis of acute mastoiditis. Further observation of the case may be necessary. For weeks, a positive reservoir sign may be the sole sign on which a diagnosis of mastoiditis can be made. The longer the time-interval—dated from spontaneous perforation of the tympanic membrane, or myringotomy—the greater is the significance of the sign; that is to say, a positive reservoir sign alone, elicited one month after perforation, is absolutely diagnostic of mastoiditis.

CASE 2.—A man of 56, the subject of diabetes, with eye complications, developed an attack of acute otitis media. I saw him four weeks later; in the interval and at the examination he was free from earache or mastoid tenderness, and the temperature throughout was normal. It was only the ear discharge which made him seek advice. After cleaning the meatus, beads of pus were observed to ooze through the perforation in the tympanic membrane, as tooth paste is expressed out of its tube. The reservoir sign was positive in ten minutes. Operation revealed a large mastoid abscess exposing the lateral sinus.

The more rapid the reaccumulation is the more urgent is the indication for immediate operation on the mastoid.

So frequently is the positive reservoir sign elicited, when sought for, that on the day this was written I operated on five consecutive cases of acute mastoiditis, in three of which the positive reservoir sign was present as the sole symptom or sign of the mastoiditis.

CASE 3.—Boy aged 6. Left ear discharge for ten days. Reservoir sign positive in 20 minutes. Temperature 99° F. No other sign.

CASE 4.—Infant aged 7 months. Right ear discharge one month. Reservoir test positive in 20 minutes. No other sign.

CASE 5.—Child aged 2½ years. Right ear discharge four weeks. Reservoir test in 20 minutes. No other sign.

In all the cases operation revealed infection of the mastoid antrum and cells.

A positive reservoir sign may be associated with a sagging of the postero-superior meatal wall. The latter sign, however, alone is diagnostic of acute mastoiditis.

The value of a positive reservoir sign has been confirmed from a consecutive series of 467 mastoid operations, performed by me during the last four years. Of this number 322 were for acute mastoiditis.

## A MODIFIED TECHNIQUE FOR THE ENUMERATION OF BLOOD PLATELETS

By H. Lempert, M.Sc. Manch., A.I.C.
TECHNICAL ASSISTANT, CLINICAL LABORATORY, ROYAL INFIRMARY, MANCHESTER

Kristenson [1] devised a method for the enumeration of blood platelets in blood taken from a vein. This was not very practical when a large number of determinations were required and the technique was later modified [2] so that blood from a finger could be used. The apparatus consisted of a white-cell pipette with the tip widened into the form of a bulb which was filled with a 6 per cent. solution of olive oil in ether. When the ether evaporated, the walls were coated with a thin layer of oil. This was said to prevent the platelets from agglutinating. For the same reason, the finger was also treated with oil. The blood was diluted approximately 1 in 12 with a diluting fluid formulated by Kristenson.[1]

I attempted to modify this method so that an ordinary white-cell pipette and a technique as simple as that for a white-cell count could be used. The diluting fluid [1] left a large number of red blood corpuscles unhæmolysed and there was a tendency for the platelets to agglutinate. Bacquero's modification [3] was tried without success.

The following modification has been found to give a uniform separation of the platelets with a complete hæmolysis of the red blood corpuscles. The platelets stain deep blue and are easily counted. The solutions required are :—

| | |
|---|---|
| A.—Sodium citrate .. .. .. .. | 1·0 g. |
| Mercuric chloride .. .. .. .. | 0·002 g. |
| Brilliant cresyl blue .. .. .. | 0·2 g. |
| Dissolved in 100 c.cm. distilled water at | 45° C. |
| B.—Urea .. .. .. .. .. | 20 g. |
| Distilled water to .. .. .. .. | 100 c.cm. |

Equal amounts of A and B are mixed when the diluting fluid is required. The mixture contains 10 per cent. urea as against 2 per cent. in the diluting fluid,[1] the other constituents remaining the same. The mixture will keep for several days but should be filtered each day. The intensity of the stain diminishes, however, due to the presence of the urea. Solutions A and B in separate glass-stoppered bottles have kept very well for nearly two years.

### TECHNIQUE

Clean a white-cell pipette with chromic acid, wash with water, and dry thoroughly before use. Mix 3 c.cm. A with 3 c.cm. B and filter or, better still, centrifuge for five minutes and then filter. Clean the finger or thumb with methylated spirits and make quite sure that it is dry before pricking with a sharp needle. A large drop of blood should be obtained with only light pressure from a tourniquet. Draw diluting fluid up to the 05 mark on the stem of the pipette and wipe the tip. Now draw blood in until the liquid reaches the 1 mark. Wipe the tip again and draw diluting fluid until the pipette is full and the blood diluted 1 in 20. Shake the pipette immediately for one minute. Leave for ten minutes for the platelets to take up the stain, and again shake continuously for two minutes before putting a drop into a scrupulously clean hæmocytometer. Place a piece of moist cotton-wool on either side of the hæmocytometer and cover with the lid of a Petri dish to prevent evaporation. Allow the platelets to settle for 20 minutes before attempting to count.

| | Modified technique. |
|---|---|
| Blood platelets per c.mm. normal blood .. .. | 236,000 .. 320,000 |
| | 254,000 .. 256,000 |
| | 256,000 .. 260,000 |
| | 330,000 .. 305,000 |

### SUMMARY

The Kristenson method for the enumeration of blood platelets has been simplified. This has entailed the formulating of a new diluting fluid. The method dispenses with the use of olive oil to prevent agglutination. When the finger shows natural excessive moisture, a few drops of a concentrated solution of paraffin wax in ether are rubbed in and a prick made through a very thin layer of wax. When the blood contains a large number of reticulocytes some difficulty is experienced in counting. This is overcome by taking about two-fifths of the stipulated amount of blood into the pipette. The blood platelets in normal counts appear to be approximately 250,000 to 350,000 per c.mm. blood. This agrees with Kristenson.[1]

I wish to thank Dr. G. E. Loveday, director of the clinical laboratory, Royal Infirmary, Manchester, Dr. J. F. Wilkinson, director of clinical investigations and research at the Royal Infirmary, and Dr. L. Wislicki, of the Victoria Memorial Jewish Hospital, Manchester, for suggestions in the preparation of this paper.

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2. " : Ibid., 1928, lxix., 227.
3. Bacquero, G.: Arch. de Card. y Hem., 1930, xi., 140.

# MEDICAL SOCIETIES

## ROYAL SOCIETY OF MEDICINE

### SECTION OF ORTHOPÆDICS

At a meeting of this section held on Jan. 15th, the chair was taken by Mr. A. H. Todd, the president. Dr. H. H. Kessler (head of the Rehabilitation Centre and Commission of Newark, New Jersey) read a paper on some problems of

### Industrial Orthopædic Surgery

The problem, he said, was common to all countries; the work in New Jersey had arisen from the visit of a legislator to the Lord Roberts memorial workshops during the war. The workman's compensation programme had been adopted some seven years previously. To-day there were rehabilitation services in 44 States; practically all supplied vocational training for the civilian disabled; many supplied prosthesis. New Jersey, in addition, provided surgical and medical rehabilitation. There was a difference between an "insured" and a "non-insured" accident. The central egoistic core of the personality had a very high value. If a low value, for example an insult, were introduced into the personality, it set up tension, manifested in the myriad forms of neurosis. It had to be thrust out, which could be done by returning the low value whence it came—blow for blow or insult for insult—or by an apology. An accident acted like such an insult or low value; hence the apology to the individual by way of compensation.

In America there was a schedule of disabilities in every State and compensation was based on general —not special—disability. The amount awarded for each injury varied in different States. The loss need not be an amputation; loss of function was taken into account. Dr. Kessler showed by slides how the disability was measured in each unit or part. Muscle power was estimated with a spring balance. Dynamometers had been discarded as unsatisfactory. Motion, strength, and coördination having been measured, the greatest loss was taken as the loss of the unit. A Colles' fracture, for example, showed 12 per cent. disability for the arm radicle and 20 per cent. for the hand radicle, as the patient had difficulty in grasping small objects. The disability of the extremity unit was therefore taken as 20 per cent. Psychological and personality factors played a great part in disability. New Jersey felt that these people could be rehabilitated and made self-supporting. The clinics were equipped with re-educational apparatus. Even if the disability could not be reduced, work was found that the patients could do. Often prosthetic apparatus helped, but very few would wear artificial arms. Most disabled workers were able to go back to the work they had done before, except after major amputations. It was not easy to train an adult to a new trade. The laboratory served also to estimate the work capacity of the individual, and to indicate his possibilities. Many of the disabled had retained their work throughout the depression. The compensation law, with its specific schedule, was a great help to the work as it determined the amount the patient might get with almost precise accuracy.

The PRESIDENT remarked on the difficulties which would be encountered in starting any similar scheme in this country and also on the urgent need for something of the kind. It was very difficult to place afresh a man who could no longer follow his original vocation. A scheme must be acceptable to injured workmen, employers, and insurance companies. He preferred, however, to emphasise the need rather than the difficulties. He asked whether the State had any authority to make a man attend the centre, and where the money came from. Insurance companies had found that the scheme paid them handsomely.

Dr. KESSLER replied that the Rehabilitation Unit was, in New Jersey, part and parcel of the Workmen's Compensation Unit and supported out of the rates and taxes. It cost some $50,000 a year. Part of this money came from the Federal Government. Some six to eight hundred men had been treated during the past year and they would have cost the State a good deal more in relief than they had during rehabilitation. If the disability could be actually reduced, the compensation would be reduced and the insurance company thus benefited. The assessment of disability was made by the State physician, and the referee put the stamp of legal approval on it.

Mr. W. MCADAM ECCLES spoke of the importance of prevention of disabling conditions by the primary treatment of industrial injuries. One of the chief problems in rehabilitation was to get the confidence of the disabled person. A great deal of surgical orthopædic work was also required. The cosmetic result was of very great importance in obtaining work. One of the difficulties in this country was that those who presided over the courts tended to think they knew as much about disability as a surgeon. In most cases the medical assessor was a great help, but was not available in the High Court. Some of the amounts awarded in the High Court were very large and caused workmen to hold out against rehabilitation in the hope of being awarded enough to buy a house. The trade-unions did not seem to want a person to get back to work or have rehabilitation treatment.

Dr. P. VERNON said there was a very fundamental difference between America and this country. Here there was no scale of disabilities and the American scales seemed very low compared with those prevailing here. The low scale encouraged the workman to seek rehabilitation. Here one judge would consider percentage disability; another would refuse to do so.

Mr. G. E. DUNNINGHAM said that there must be education and that it must come from the medical profession. Pain constituted a great difficulty; nobody could see or estimate pain or discomfort. His doctor told the court that the man had pain and the judge awarded compensation. A definite scheme of compensation would be a great help. Without a change of circumstances Dr. Kessler's scheme would not work here.

Mr. C. HOPE CARLTON said that the reason why there was no such work here as in America and Holland was threefold, and lay in social and industrial conditions. The man was always wondering what he would get as a lump sum, and the change when this point was settled was amazing. Secondly, patients dragged on in misery because of the variety of agencies from which they could obtain certificates of disability; they rang the changes on different hospital surgeons and panel doctors. Thirdly, much blame lay with the insurance societies which cut their losses, paid the 30*s*. a week, and did not care whether the man got better or not.

Dr. C. E. MOORE, speaking from his experience with the L.M.S. Railway Co., said that rehabilitation centres would undoubtedly reduce the enormous wastage going on in this country. We should never get any further until the conflicting evidence of medical witnesses was eliminated. The only way to get rid of injustice was to have centres where functional ability could be tested with absolute certainty. The psychological element could not be excluded.

Mr. S. A. MALKIN asked how the rehabilitation centres were linked with the hospitals and whether they were also treatment centres. The interval between the time when the patient was fit and the time when work was available was a great difficulty; how was it bridged?

Dr. KESSLER, in reply, said that rehabilitation clinics did not undertake emergency or fresh treatment. A small percentage of cases came from hospitals but 70 per cent. from the compensation bureau. The director of the clinic was on the staff of several hospitals, thus effecting a valuable link. Many of the patients needed surgical intervention. America had found the county court method of adjudicating claims quite inadequate and had given it up. A judge, asked recently how he made his decisions, had replied: "By intuitive correlation." Not every case was successful but the scheme was a tool whereby an otherwise insoluble problem might be tackled. The referee had authority and his decision could only be reviewed on appeal in respect of law, and not in respect of fact. Rehabilitation paid, and it could be applied in England as well as in America.

The PRESIDENT said that insurance companies did not encourage treatment, partly because they were not too sure of its results. Patients did not have

expert investigation early enough. It might be that there were not enough real experts available. He suggested that a conference between medical men and insurance companies might lead to a schedule of disabilities and improved conditions.

Dr. C. B. HEALD said that the London County Council had decided to start a small rehabilitation scheme and asked what equipment would be necessary.

Dr. KESSLER answered that $1000 had started their clinic.

## ABERDEEN MEDICO-CHIRURGICAL SOCIETY

A CLINICAL meeting of this society was held in the Royal Aberdeen Hospital for Sick Children on Jan. 10th, the president, Dr. WILLIAM BROWN, being in the chair.

The PRESIDENT showed three cases of communicating internal hydrocephalus in which the diagnosis was reached by the intraventricular injection of indigo-carmine solution. The patients had been treated by repeated ventricular and/or lumbar puncture together with the administration of hypertonic rectal salines. Lumbar or ventricular puncture was done according to the intracranial pressure, as estimated by the state of the fontanelles. He pleaded for submission of these cases to treatment early since there seemed to be hope of improvement.

Dr. JOHN CRAIG gave details of two children in which "black eyes" were a prominent feature. One was a case of infantile scurvy; in the second case the "black eye" was due to secondary deposits in the skull and orbit from a neuroblastoma of the suprarenal gland.

Mr. ALEX MITCHELL showed a girl with symptoms suggestive of cervical rib on the left side. X rays failed to show any evidence of cervical rib and the symptoms were completely relieved by the division of the scalenus anticus muscle. He also showed a boy aged 6 who had had hæmaturia from a neoplasm of the right kidney. Laparotomy showed the tumour to be inoperable. The patient had been treated with deep X rays with considerable diminution in the size of the tumour and cessation of the hæmaturia. Mr. Mitchell also demonstrated an apparatus for the gradual reduction of congenital dislocation of the hip and showed a series of skiagrams from a case in which reduction had been obtained. The process was a very gradual one and in the case shown had taken four months before complete reduction was obtained.

Mr. N. J. LOGIE for Mr. A. FOWLER demonstrated a series of children who had had fractures of the forearm bones treated by open operation. The X ray plates and the functional results clearly showed the excellence of the method.

Dr. H. ROSS SOUPER gave details of a case of acute otitis media with meningitis and death within five days of the first symptoms; he also described a case of acute otitis media with meningeal symptoms which rapidly subsided after paracentesis.

Mr. J. H. OTTY described three cases of otitic meningitis resulting from chronic suppurative otitis media. Two cases recovered—one following translabyrinthine drainage; the other following radical mastoidectomy. In the fatal case meningitis occurred 15 days after a radical mastoid operation. Hæmolytic streptococci were obtained from the cerebrospinal fluid of the fatal case, but no organisms were recovered from examination of the fluid in the other cases.

# NEW INVENTIONS

## A TEACHING STETHOSCOPE

THE stethoscope illustrated here consists of a scientifically constructed sound chamber which incorporates a diaphragm and tension wire designed to transmit heart sounds which are mostly within the bass range of piano notes. Although the intensity of the sounds is diminished to some extent, the quality is preserved, and is comparable to that which a student hears when using his own binaural stethoscope. Six observers (the instructor and five students) may auscultate the chest at the same time, and in this way the teacher is able to emphasise certain characteristics as they occur. The use of the instrument thus aids the instruction of students in the first principles of auscultation applied to both normal and adventitious heart and breath sounds, while it provides the means of knowing that the student has heard the particular abnormality to which his attention has been drawn by his teacher. The stethoscope also enables each student among a moderately large class to elicit a particular auscultatory sign in an ill patient without causing the discomfort involved by repeated individual examinations.

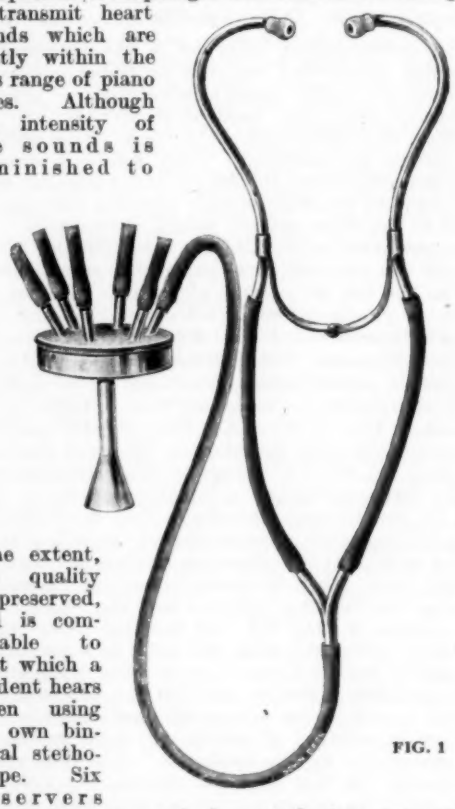

FIG. 1

FIG. 2

The instrument has been constructed for me by Messrs. Down Bros., 21, St. Thomas's-street, S.E. 1.

London Hospital, E. WILLIAM EVANS, M.D. Lond.

# REVIEWS AND NOTICES OF BOOKS

## Le décollement de la rétine

By J. GONIN, Professor of Clinical Ophthalmology at the University of Lausanne. Lausanne: Librairie Payot et Cie. 1934. Pp. 279. 50 Swiss francs.

THE extraordinary advance in the treatment of detached retina that we owe to Gonin makes the publication of this comprehensive work an event in ophthalmology. The treatise is divided into two sections, the first on the pathogenesis of detachment, the second on treatment; there follows a series of 33 plates illustrating the details of detachment and a collection of ophthalmoscopic pictures showing the shape of the holes and the results of treatment. The literature of retinal detachment is formidable. Gonin himself has contributed 41 papers to various periodicals in the last 40 years, and during the last five years the number of important communications from other authors, of which a list is here given, is over 300.

By "idiopathic" detachment is meant detachments that are not secondary to some other condition, such as tumour or organised hæmorrhage in the vitreous. This work teaches that, strictly speaking, all detachments are secondary in the sense that they are preceded by a shrinkage of the gelatinous part of the vitreous, leaving a liquid occupying a large part of the vitreous chamber. This itself may be secondary to some inflammation of the ciliary body. At any rate, there are cells or membranes not normally present and, what is more important, adhesions between the shrunken vitreous and the retina itself. The results of this and the mechanism by which the retina is dragged upon and holes in it are formed are worked out by Gonin in a way which might not be so convincing were it not that the practical conclusion to which his arguments lead—namely, the primary importance of sealing the hole or holes—has proved the key to treatment. The theory is a modification of that first put forward by Leber in 1882, but it is generally acknowledged that it is to Gonin that we owe its application. The essential lesion is the formation of the hole, and this may occur at the point where an old retino-choroiditis has left adhesions; or holes may be the result of tearing away the peripheral anterior attachments of the retina—disinsertions, as Gonin terms them, or to use a phrase which Duke-Elder prefers, "dialyses." In practice the first essential is the exact location of the hole or holes. Clinically, Gonin insists, failure to find it is due either to lack of experience in recognising the hole when seen or to insufficient search. Of course, the media must be sufficiently clear for a complete ophthalmoscopic examination.

When the hole has been found the next task is to locate it so that the corresponding spot on the sclera may be defined. Gonin's own procedure is then to apply the thermo-cautery to the spot. The fluid having been evacuated an inflammatory reaction is caused which, if the hole has been successfully located, effectively seals it. Other methods of effecting the same object have been introduced since Gonin first made his reputation, and instead of piercing the sclera with the cautery the operations most often performed at the present time depend on diathermy, either by the method of Larsson or by that of Safar. All methods can produce successes if properly applied and adapted to the particular case. Not all cases, however, are susceptible of cure. During the years 1929 to 1931 Gonin found that out of 300 "idiopathic" detachments 78 were unsuitable for operation. Of these, 30 had opacities of the media preventing a sufficient view of the fundus, and in 21 the hole was too large to afford a prospect of success. Other contra-indications were low tension of the globe, the bad state of general health of the patient, the extreme posterior position of the hole making it too difficult of access, and, in some cases, the fact that the detachment appeared to be sufficiently isolated by adhesions to make the utility of operation doubtful. Of those operated on just over half were tabled as successes; of those treated not more than three weeks from the first symptoms, 66 per cent. were successful, the figure falling to 51 per cent. of those of duration three weeks to three months, and 37 per cent. for those of a still longer duration. Of the 118 patients cured 65 were cured with a single operation, the rest with two or more. Of the failures the commonest cause was either the size of the hole or the multiplicity of holes. There were 11 cases of post-operative hæmorrhage. Other causes of failure were lack of discipline on the part of the patient, want of transparency in the media, and the formation of a secondary hole near the cicatrix of the one successfully closed. These statistics are comparable with those of Shapland, who tabulated the Moorfields results up to March, 1932 (Trans. Ophth. Soc., 1932, lii., 170).

Taken together they indicate that although the operation for detachment is not applicable to all cases and can only be undertaken by specialists familiar with a technique that is new, yet in suitable cases, and especially in recent ones, it has now become one of the really hopeful operations in ophthalmic surgery. The present position may be contrasted with that of five years ago when, in a leading article in THE LANCET quoted by Gonin, it was stated without fear of contradiction that "there are few ophthalmic surgeons who cannot count on the fingers of one hand the cases of cure of detached retina within their own personal experience."[1]

Towards the end of his treatise the author propounds and answers three questions: (1) Should one operate? (2) At what period should one operate? (3) How should one operate? In response to the last question he shows that he is not wedded exclusively to his original technique, but is convinced that when properly applied all the methods can produce successes. Whatever such further improvements the future may show it is clear that the main credit for this revolution in treatment properly belongs to the author of this important monograph.

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## A Text-book of Histology

By E. V. COWDRY, Professor of Cytology in the School of Medicine, Washington University, St. Louis, Mo. London: Henry Kimpton. 1934. Pp. 503. 25s.

THERE is admittedly no subject in the medical students' curriculum where the text-book plays a less essential part than in histology. Descriptions of histological structure usually make tedious reading, and practical work with the microscope is a pleasanter and more effective way of becoming familiar with the subject. Probably most medical students appreciate this and leave their text-books largely unread; but there continues to be a substantial demand for such books, many of which are no more than laborious

[1] THE LANCET, 1929, ii., 1202.

attempts to describe things which must be seen to be understood. Others however are of value not only to students but to teachers. This one is planned on original lines. The author has more or less dispensed with purely topographical descriptions and has aimed at a study of the development and purpose of tissues. Much physiology has been introduced, which is useful, in that it enables the student to coördinate his various studies. Prof. Cowdry aims at teaching by inspiration, and his book, which is essentially a review of research work in histology, furnishes an immense amount of fascinating information, which could hardly fail to induce the student to examine tissues for himself.

The plan of study presents some important variations from the one usually adopted. Special attention has been paid to the requirements of the medical student, and the organs and tissues of most vital importance to medicine have been given priority. So far as possible the subject has been treated as an integral part of the medical curriculum rather than as an independent science. The work opens with a study of the blood vascular system which provides the central theme of the work, but considerable attention is paid to the endocrine and reproductive systems, where histological researches have played a large part in the advancement of knowledge. In the illustrations, little or no attempt has been made at the reproduction of elaborate histological pictures, for these merely show what the student must be taught to find for himself under the microscope. The pictures are for the most part diagrammatic rather than picturesque. Many of them are simple pen drawings, which serve their purpose admirably. The book contains an unusually large amount of information for its size, and the bibliography has about a thousand references. It is undoubtedly a publication of considerable importance, and not only teachers of histology but those concerned with every branch of medical education would be well advised to give it attention.

## Prolapsus du rectum

Par CARRASCO. Préface du Prof. HARTMANN. Paris: Masson et Cie. 1934. Pp. 196. Fr.35.

THIS monograph is devoted entirely to a discussion of prolapse of the rectum. In the first three chapters we find a brief recapitulation of the ætiology and anatomical varieties, and an account of the many theories of the origin of prolapse, including the theory of Moschowitz that complete prolapse is due to the descent and hernial protrusion of the pouch of Douglas. Next comes a study of the symptoms of prolapse, including the important complications such as irreducibility, strangulation, and rupture. The remainder of the book deals with treatment, which is divided into main subdivisions such as cauterisation, injection of sclerosing solutions, amputation, abdominal suspension or fixation operations, and the rectopexy operations described by Sick and by Lockhart-Mummery. We notice that several operations to close the pouch of Douglas are described, of which the method of Quénu and Duval (1910) was apparently the earliest. An extension of this method, which is commonly known in English-speaking countries as the Moschowitz operation, consisting in closure of the pouch of Douglas by placing several tiers of silk or thread sutures circularly round the pelvis from below upwards, is not specifically mentioned. Finally, a number of plastic operations are described, such as pleating operations to tighten the external sphincter, plication of the rectum, or its suture to the sacrum. Many of the methods described are only of historical interest, but the compilation is a valuable one and is a testimony to the industry of its author. A complete bibliography for the last 30 years is given and the more important operations are well illustrated.

In the final page the author points out the importance of assessing each case of rectal prolapse on its own merits, particularly in regard to age, sex, and general condition of the patient, the duration and degree of the prolapse. In children treatment is usually a simple matter, but in adults it is much more difficult. Surgeons dealing with cases of rectal prolapse will appreciate the orderly arrangement of this book, the bibliography, and the clear description of standard operations. Many illustrative case reports with their final results are given.

## Modern Clinical Syphilology

By JOHN H. STOKES, M.D., Duhring Professor of Dermatology and Syphilology in the School of Medicine, University of Pennsylvania. With ten collaborators. London: W. B. Saunders Co., Ltd. 1934. Pp. 1400. 50*s*.

DURING the eight years which have elapsed since the publication of the first edition of Prof. Stokes's book, great advances have been made in many aspects of the subject of syphilology, the consideration of which has necessitated a very notable increase in the size of the volume—from 1144 pages and 865 illustrations and text figures in the first edition to 1400 pages and 973 illustrations in the present edition. In this edition 15 of the original 23 chapters have been completely rewritten. Among the subjects which have been more particularly expanded in the light of recent work are the "cure" of syphilis; relapse and reinfection conceptions from the clinical and experimental points of view; and the value of pathological tests, especially the serological, in the light of the precipitation tests and the League of Nations' comparisons. In the domain of treatment, much new material has been added, including a discussion of the relative value of the various arsenobenzene preparations; a section on stovarsol (acetarsone, spirocid, orarsan); fuller consideration of the use of bismuth and tryparsamide; and a complete review of the treatment of early syphilis "in terms of definite systems, and the conclusions established by the elaborate investigations of the past five years." The author has utilised the valuable results obtained by the Coöperative Clinic Group and the United States Public Health Service from the records of 75,000 cases of syphilis in all its aspects. He goes fully into the comparative value of continuous versus intermittent treatment, being strongly in favour of continuous treatment in early syphilis. The need to examine the cerebro-spinal fluid in every case at the proper time during the course of treatment is strongly emphasised. Neurosyphilis in all its aspects is well covered; on the most vexed question in this connexion Prof. Stokes holds that there is no convincing evidence that the adequate and effective use of arsenicals predisposes in any way to syphilis of the nervous system, but that there is abundant evidence that an increase in the incidence of neurosyphilis is likely to follow inadequate use of the arsphenamines leading to neuro-recurrence. The prevention of congenital syphilis by the treatment of the expectant mother, the control of infectivity in all its aspects, including marriage, and the organisation of treatment centres and other public health phases of modern

syphilology all receive adequate attention. As in the first edition, the principal author has been ably assisted by a group of collaborators who have made the work a "monographic presentation of a coöperative effort." The result is a complete and authoritative exposition of the subject.

## Davis's Applied Anatomy

Ninth edition. Revised by GEORGE P. MULLER, M.D., Professor of Clinical Surgery, Graduate School of Medicine, University of Pennsylvania. Philadelphia and London: J. B. Lippincott Co. 1934. Pp. 717. 42*s*.

THIS well-known text-book must be of much value to American students since this is its ninth edition, and Dr. Muller has been able to obtain the help of a large number of distinguished collaborators, but it is difficult to see where it could be usefully fitted into the training of an English undergraduate. A text-book of "applied anatomy" should certainly exclude anatomical minutiæ which are of no practical significance, but it should describe clearly the anatomy which *is* of fundamental importance in clinical examination or in planning surgical operations. This book satisfies the first requirement but fails in its lack of references to the relation of structure to function, and to the importance of anatomical features influencing pathological processes and therapeutic methods. The best sections are those on the limbs and the thorax, and the illustrations are beautifully done throughout the work. But the sections on the applied anatomy of the skull and of the abdomen call for considerable improvement. There is no reference to cisternal puncture, and very little to the nerve-supply and lymphatic drainage of the tongue, the formation of pharyngeal pouches, the spread of lymphatic infection from the abdomen to the neck, or to the recent work on the exact course of the nerves in the anterior abdominal wall which has an important bearing on the planning of abdominal incisions. Many of the views expressed on fractures of the skull and on its blood-supply and some of the references to cranial operations are obsolete. It is a pity that in a student's text-book mistakes in proper names like "Battles'" and "Rawlings," and errors in setting up type, as on pages 562 and 563, should be allowed to occur.

The book is of value as a guide to the pure anatomy which every clinician should try to remember, though for this purpose alone it is unduly long; but it does not make clear the fundamental importance of anatomy in clinical practice.

## Melancholia in Everyday Practice

By EDWIN L. HOPEWELL-ASH, M.D. London: John Bale, Sons and Danielsson. 1934. Pp. 136. 7*s*. 6*d*.

THE doctors in general practice to whom this little book is addressed will doubtless find in it many useful reminders of the frequency of depressive and other forms of mental disorder among those who visit their consulting rooms. The presentation, in spite of a frequent assertion of personal opinion—"I strongly advocate"; "It is my experience that . . ."—contains nothing that is new; most of it is along earlier Kraepelinian lines, with tables of symptoms to facilitate diagnosis, discussions as to classification, and some rather naïve skating over dangerous and obscure places in modern psychiatry. Psychiatrists may wonder why such a book should be published when there are already available excellent standard works such as those quoted by the author. The book is, however, obviously based on wide practical experience, and constitutes a sensible, if rather narrow, account of the forms of depressive illness that may be seen outside mental hospitals.

## Sang et organes hémopoiétiques

By A. TOURAINE, Médecin des Hôpitaux de Paris. Paris: Masson et Cie. 1934. Pp. 258. Fr.30.

THIS book is stated in the preface to be intended for the student though it is hoped that the practitioner will find it helpful. The development and morphology of the cells of the blood are clearly described. Methods of examining the blood are discussed and there is a detailed account of certain blood diseases. Idiopathic hypochromic anæmia, a common disease, is not, however, mentioned; there is no discussion of the significance of gastric analysis in either the diagnosis or ætiology of anæmias, and the cause of Addisonian pernicious anæmia is said to be completely unknown, recent work on extrinsic and intrinsic factors being ignored. Anæmia associated with pregnancy is described as rare and when it occurs it is said to be commonly of the pernicious type. It is suggested that iron should be given in small doses to all anæmias, and no differentiation is made between the type of anæmia that will respond to iron, and that which will respond to liver. The book cannot be recommended.

## St. Bartholomew's Hospital Reports

Vol. LXVII. London: John Murray. 1934. Pp. 279. 15*s*.

THE group of papers on goitre by Prof. Francis Fraser, Sir Thomas Dunhill, and Dr. A. W. Spence were the subject of comment in THE LANCET last week. A symposium on the problem of peptic ulcer in this issue is chiefly concerned with the results of the treatment of this condition as judged by the reports from the hospital follow-up department, but Prof. H. H. Woollard and Prof. E. H. Kettle supply critical reviews respectively of the anatomical and pathological considerations which have a bearing on the nature of the process of ulceration. Dr. Geoffrey Bourne has written a short account of his experience of duodenal feeding. Mr. Ronald W. Raven has made a laborious analysis of 357 cases of chronic gastric ulcer and 272 cases of chronic duodenal ulcer which have been followed up since 1929. Though he has made several important deductions he has not been able to give a concise answer to the question of when surgery is required as an adjuvant to medical treatment, and a disquieting observation is the high total mortality-rate for the surgical treatment of chronic gastric ulcer in this series. Lord Horder, in an introduction to the symposium, makes a plea for gastro-enterostomy as the appropriate operation for gastric ulcer: his arguments are not supported by Mr. Raven's statistics. Mr. Girling Ball, reviewing 58 of his own cases, advocates partial gastrectomy as the procedure more likely to ensure a good after-result. A paper by Dr. A. Q. Wells showing the importance of $\beta$-hydroxybutyric acid as the active agent in the treatment of urinary infections by ketogenic diet; two papers by Dr. I. J. Wood and Dr. A. W. Franklin on the detailed investigation and treatment of some unusually interesting cases of anæmia in infancy; and a biographical note in memory of William Foster Cross, consulting anæsthetist, who was for many years a popular and greatly valued member of the hospital staff, complete the volume. The thinner paper used for this volume has considerably improved its appearance.

THE LANCET

*LONDON: SATURDAY, JANUARY 19, 1935*

## MALARIA IN CEYLON

NEWS of a great malaria epidemic in Ceylon, with half a million cases and a heavy mortality, may seem at first surprising. The island has never had the name of being unhealthy; no one has ever called it a "white man's grave"; indeed, it was chosen for reasons of salubrity as a place to which prisoners were sent by the British Government during the South African War. To most people Ceylon is a beautiful, fertile, and prosperous island, an important tea-growing country, whose inhabitants, well known in our inns of court and medical schools, are obviously an intellectual race and heirs of an ancient culture. Its buried cities are sometimes mentioned but are seldom regarded as anything more than an additional and picturesque attraction to tourists.

Generally speaking these impressions are correct, but there is a grim background, not merely in the present epidemic but in the grip which malaria has maintained on a large part of Ceylon for some eight centuries. The healthy, flourishing parts of the land are the south and west lowlands and the central mountain mass; they receive the full force of the south-west monsoon, their rainfall ranges from 40 to 100 in. a year, and their population, of some 400 people per square mile, lives largely on little gardens surrounded by fruit trees and flowering shrubs, cultivating the rice fields. In strong contrast to these are the north and east parts of the island. They too were once tropical gardens; there were great cities, and a great irrigation system, some of whose tanks are as large as the largest reservoirs of the Metropolitan Water Board. To-day the ruins of these cities are buried in jungle; their inhabitants are the leopard, the wild pig, the tiger, and the elephant; the great irrigation system remains, but the tanks are silent except for the call of the water-birds. Only in small patches here and there is the land cultivated. In place of an educated and prosperous people, a few miserable wretches, half-starved and sodden with malaria, cling to a fretted thread of life. So it has been since the Tamils from southern India drove the Sinhalese out of their cities and fields into the central mountains about the twelfth century. After the invaders left, the remnant of the inhabitants returned to their homes, but they were unable to recreate their prosperity—were able indeed to do little but die of the malaria now firmly established in the land. In the centuries that followed the Sinhalese have over and over again tried to colonise these areas, and failed. In Africa and India are to be found large numbers of people who can tolerate the malaria parasite sufficiently to live in places no less malarial than this part of Ceylon; but perhaps it has taken them many thousands of years to acquire this tolerance. Be that as it may, 800 years have not given the Sinhalese a corresponding resistance. Nor does the European attempt to cultivate this area; for him too the land is practically uninhabitable: it would be a white man's grave were he to do so. And just because malaria reigns unchallenged, the land is jungle-bound. It is as if it did not exist, and men forget how near the enemy is to their gates. But from time to time there is a drought in the south, and the drought conditions of the north are reproduced in other parts of the island. What exactly happens is not fully known, but malaria then spreads south and west, even up the slopes of the mountains for 2000 or 3000 ft., and death follows in its wake. For want of water to irrigate the fields, and want of strength to till and harvest the land, the crops fail and famine follows sickness.

Malaria in Ceylon is a major problem—the major problem of the country. If it is to be overcome an organisation must be created which will study its every aspect, and on the facts discovered build a system for preventing the disease. The British Government have given the people of Ceylon a large measure of self-government, and we may be sure that if Ceylon asks for help it will be given freely. In no better way could the Ceylonese prove their fitness for rule, and love of their native country, than by working to deliver it from this pestilence.

## LEFT-HANDEDNESS AND STAMMER

A MEMORANDUM concerning left-handed children, recently issued by the London County Council Education Committee, advises that some attempt should be made, for practical reasons, to encourage all children to use the right hand, but points out that pressure, especially by punishment or ridicule, may produce a harmful degree of emotional disturbance resulting in nervous symptoms, including stammering. This authoritative warning should settle a problem that has vexed many teachers who, in accordance with modern tendencies, had begun to ask whether a left-handed child might not, after all, be given the right to follow his own habit.

The undoubted relationship of corrected left-handedness and stammering is capable of two explanations which at first sight appear mutually exclusive—one physiological, the other psychological. The physiological explanation was presented in our pages last year by Dr. CHARLES J. MACALISTER,[1] who follows the general belief that the cerebral speech centre is left-sided in right-handed people and the opposite in left-handers, this belief being based upon observed results of cerebral disease. It is, however, not always true, and he cites MOUTIER as finding that the rule sometimes fails both in right- and left-handed subjects. Of right-handers with the speech centre apparently upon the same side MOUTIER makes

[1] Left-handedness, THE LANCET, 1934, i., 1151–1153.

the observation that many of the relatives were left-handed, so that the subjects might be regarded as physiological left-handers though manifest right-handers. We can, nevertheless, accept as generally correct the location of a right-sided speech centre in left-handers, and assume that centre to be in some way functionally related to the action of the dominant left hand. But the corresponding area of the other hemisphere does not remain idle; Dr. MACALISTER speaks of one side as containing the leading and the other the automatic centre, and Sir GRAFTON ELLIOT SMITH, in his recent book "The Evolution of Man," carried this conception a step forward by pointing out that, whilst one side of the brain is becoming perfected in the control of certain actions such as writing, the other side is preparing the mirror-like control of the same actions; we see as a result the ease with which people can at the first attempt write mirror-fashion with the left hand. The left-hander has thus at an early age used his right hemisphere both for speech and for left-hand movements, whilst the left hemisphere has become automatic and been trained mirror-wise. If the left-hander is now forced to become right-handed this left hemisphere must renounce its automatism, take the lead, and reverse its control from mirror-wise to direct. The difficulty of this transposition of cerebral functions results in stammer. In favour of this straightforward anatomical explanation is the fact that the majority of cases with transposition of viscera also show left-handedness. Further support comes from the claim of ELLIOT SMITH that left-handedness is indicated by a special asymmetry of the lunate sulcus on the two sides, though his deductions rest upon measurements of the humerus and clavicle as indicators of left-handedness and do not seem to have been confirmed by post-mortem study of the brains of known left-handers. Dr. MACALISTER notes that the stammers arising independently of association with left-handedness cannot be explained on these anatomical grounds and for these he is willing to accept a psychological explanation.

A psychological attack upon the whole problem was made by Mr. W. S. INMAN ten years ago.[2] He notes the common attitude of intolerance towards left-handedness in the child, though in the adult it is accepted as a more or less interesting peculiarity; and he points out the familial occurrence of the trio of squint, stammer, and left-handedness. But the left-handedness, he says, is rarely complete in the way that right-handedness is; many so-called left-handers are ambidexterous, and he gives examples, which could be multiplied by any observer, of isolated and peculiar left-handed activities that can with difficulty or not at all be ascribed to details of cerebral structure. Most important is his description of the temperament of the left-hander, who is, he says, obstinate and independent, yet generally calm and deliberate in going his own road, though resentful of injustice to himself or others. This temperamental make-up of the left-hander being assumed, the question arises whether it results from the possession of a peculiarity that marks him as different from his fellows or whether the peculiarity is adopted as a symbolic manifestation of his temperamental characteristics. This question Mr. INMAN leaves open, though he gives an example of an apparent attempt at left-handedness as a demonstration of childish negativism, which suggests that left handed dealing at cards—one of the commonest isolated left-handed activities—is perhaps the stabilisation of an initial protest against the apparently irrational rigour of the game. That his view of the left-hander's temperament is not new is shown by the Old Testament story of Ehud, whose bloodthirsty single-mindedness and hatred of tyranny are plainly regarded as marks of "a man left-handed." The symbolical values of left-handedness being granted, it may be supposed that a compulsory change is felt as a successful attack upon the personality, upon the right to do as one will with one's own, and that the stammer comes as a protest or a token of defeat. The application of Occam's razor now gives us a single theory that brings the stammer of the compulsorily converted left-hander into the same category as the other emotionally induced stammers, and at the same time allows of weight being given to a primary anatomical foundation of congenital left-handedness.

[2] An Inquiry into the Origin of Squint, Left-handedness, and Stammer, THE LANCET, 1924, ii., 211–214.

## BONE GRAFTS

THE behaviour of transplanted bone is still debatable. In the formidable mass of writings about it those of OLLIER in France in 1867 and MACEWEN in Great Britain in 1912 are outstanding to this day. And in spite of all the records of careful observation the pronouncements even of the last year do not altogether agree on the rôle of the bone graft in osseous regeneration and on its own ultimate fate. The purposes for which bone is nowadays transplanted are, broadly speaking, to promote the healing of fractures in which fibrous or cartilaginous pseudarthrosis has arisen; to replace bone that has been excised (as in radical resection for osteomyelitis); to bridge defects; and, finally, to cause artificial ankylosis in such conditions as tuberculosis of the vertebræ or of the knee-joint. For all these purposes transplantation has been a notable success: new bone has been found replacing excised bone, has united fragments across a pseudarthrosis, and has firmly ankylosed diseased joints. The questions that arise concern the origin of this new bone and its relationship to the graft. Does the graft live, become revascularised, and grow? Is the transplantation of living bone cells the essential part of the process? Or does the graft serve only as a scaffold and a source of calcium, the osseous regeneration occurring solely in the connective tissues forming the bed of the graft? Are the cells of the periosteum, as OLLIER taught, the active tissue; or was MACEWEN right in his view of the periosteum as a limiting membrane without powers of forming bone?

Three recent papers on bone transplantation approach it from different angles. Dr. WILLIAM J.

STEWART,[1] of Chicago University, has experimented on the efficacy of various substances in regenerating bone in defects artificially produced in healthy dogs. He found that bags of calcium salt and boiled bone were ineffective, whereas chips of fresh bone (referred to as "live" bone) led to bridging of the gap by active osseous growth. Two comments here are necessary: it must not be assumed that conditions in an artificial defect are the same as in an ununited fracture, where the bone-ends are placed in at least moderately accurate apposition; secondly, very little is known about the chemistry of calcium absorption and redeposition, and it is possible that the calcium in the fascial bags and in the boiled bone is in a form that cannot be used by the tissues. The monograph by Dr. SVANTE ORELL,[2] from the clinic for surgical tuberculosis at the St. Göran Krankenhaus in Stockholm, is of even greater interest; for he has found a very ingenious method of studying transplantation in the human subject. The Albee operation for tuberculosis of the spine involves the removal of a long piece of bone from the tibia, and ORELL has implanted in the resulting tibial defects grafts of various types of bone, later cutting down on the site of operation and excising tissue for histological examination. Some of the grafts he placed subcutaneously, others subperiosteally. Sometimes he used chips of fresh living bone, sometimes boiled bone; and in a number of cases he implanted a specially prepared bone, which he terms "os purum," prepared by removing fat, periosteum, marrow, and the cellular contents of the Haversian canals. Regeneration of bone in the tibial defect followed all these procedures. The next step in the experiments was to implant os purum under the periosteum of the intact tibia, and here the result was active formation of a somewhat fragile type of bone, which is termed "os novum." This newly formed bone was then successfully transplanted into the spine (as an Albee graft), or elsewhere, and led to active bone growth in its new environment; great success moreover attended the transplantation, side by side, of os purum and os novum.

ORELL'S comments also are important. He points out that the comparatively small grafts generally used in animal experiments may not behave in the same way as the large graft often required in surgical practice; the centre of a large graft is not easily vascularised, and necrosis is probable. This was one of the reasons that led him to direct study on patients. He believes that the essential process in bone regeneration is cellular activity. When fresh untreated bone is transplanted the cells in the Haversian canals, under the periosteum and in the marrow, play the chief part, so long as the vascularity of the bed of the graft is sufficient to assure their nutrition. Reabsorption of the bony framework is due to this cellular activity. The results ORELL has obtained with bone freed of cellular content have convinced him, however, that bone regeneration is not *dependent* on the presence of living cells in the graft. For certain purposes he prefers os purum; it is a firmer substance to use where splinting of the bone-ends is to be a function of the graft, and, owing to the absence of cellular material, it is reabsorbed more slowly. His view is that under the stimulus of os purum the cells of the surrounding tissues take on bone-forming activity; they grow unimpeded into the Haversian canals and into the interstices of the bone, for these are free of fat, connective tissue, and albuminous material; and though the process of regeneration is slower than with the use of fresh bone or os novum, it is none the less sure. Finally we come to the question of the massive graft, inserted to replace a large part of the shaft of a long bone which has been excised for disease or is congenitally deficient. Dr. MAXWELL HARBIN and Dr. K. E. LIBER[3] of Cleveland, Ohio, have made a special study of this type of graft and conclude that massive transplants in large part live as such, taking on active growth. They give one striking example of the transplantation of the upper part of a fibula to take the place of the head, neck, and upper third of the humerus. The grafted bone joined the humeral shaft, was fractured some months later, and united with the help of osteoperiosteal chip grafts. At the end of a year it was found to be completely revascularised.

The bone graft may be employed (1) as an internal splint, for which purpose it has obvious advantages over foreign bodies such as plates and screws, which by causing local hyperæmia may delay union and work loose; (2) as a scaffolding on which new bone may form by a process of "creeping substitution"—to use HARBIN'S phrase; (3) as a source of local calcium surcharge; or (4) as a source of living bone cells. The surgeon will decide in his own mind in which capacity he is using the graft, and modify his technique according to the decision.

[1] Surg., Gyn., and Obst., December, 1934, p. 867.
[2] Orell, S.: Studien über Knochenimplantation und Knochenneubildung, Acta Chir. Scand., 1934, vol. lxxiv., Suppl. XXXI.

## THE CENTRAL MIDWIVES BOARD

AT a time when the care of maternity is in the public mind as never before it is a happy fortuity that the President of the British College of Obstetricians and Gynæcologists should also preside at the Central Midwives Board. The report of the Board just issued states the astonishing fact that there are 55,928 women on the Midwives Roll, 3056 more than in the previous year, while of these only 17,789 notified their intention to practise. The percentage of trained midwives who practise as such is estimated in the report at 27·4 of the trained women on the roll. Those entering for the examination have done so more light-heartedly than usual in the year under review, for the percentage of failure was 21·7 against 17·7 in the previous year. Liverpool and Manchester have long had a large proportion of rejected candidates, and Leeds has now joined them, while Newcastle-on-Tyne retains its high standard of success. Very few charges of negligence or misconduct were dealt with during the year; of the 16 cases only 7 resulted in immediate removal from the roll. While the report is chiefly of an administrative nature the printed answers to some burning questions throw light on the midwife's daily routine. Two supervising authorities asked whether midwives were permitted to administer chloroform capsules; as the rules stand at present the administration of chloroform by the midwife, other than under medical direction, is outside her province. The Board did not see its way to enjoin the use of masks and rubber gloves by the midwife.

[3] Surg., Gyn., and Obst., August, 1934, p. 149.

# ANNOTATIONS

## MEDICAL SOCIETIES

IN his opening address at the Harveian Society's centenary meeting a few years ago,[1] Sir Raymond Crawfurd spoke of the diffusion of knowledge as the primary function of a medical society. Quite recently Dr. H. Bruce Low, in a presidential address to the Newcastle and Northern Counties Medical Society, told his hearers[2] that the objects of their ancient and honourable society were set out in the rules under five heads: exhibition of cases and of specimens, discussions, publication of a journal, social meetings. We prefer to regard these as the means to an end rather than the end itself to which the Newcastle society or any other society of medical men should direct its energies, and we are not wholly satisfied that in speaking of the "diffusion" of knowledge we fully express the true aim. Diffusion implies a thinning out, the spreading of a fixed quantity over the largest possible space. It is a term very applicable to gases, which diffuse the more readily when heated and do so with a rapidity which varies inversely with the square root of their gravity. Any mental association between the transactions of a medical society and the behaviour of heated gas or of vapours of insubstantial gravity appears to us inapt. "Propagation" on the other hand, implies increase and multiplication, and requires a forgathering, a *coeundi quiddam*, a fertilising agent, and a material to be fertilised, and so better expresses what we believe to be the objective that should be sought by any society of learned men. Medical societies can best promote the propagation of medical knowledge by providing a level ground and a common meeting place for all ranks, types, classes, and shades of medical opinion. There the specialist can disclose the results of his ever-deepening study of an ever-narrowing field. There the general practitioner can draw attention to his oft-repeated observations. We would fain see medical societies borrow the legend from the portal of Toc H: "Abandon rank all ye who enter here." We all rightly admire great men, but it encourages us if we can catch glimpses of them when they are not busy being great and learn that, after all, they are men of like passions with us. If they are really great they need not fear this close inspection, and we on our side are given a delectable opportunity of "discerning the cunning from the uncunning of physic and surgery." At table, where they talk "in profuse strains of unpremeditated art," the great may teach us as much as in their most solemn pontifications.

Only the idols with feet of clay have need to watch their step, and no man who is truly great is diminished by rubbing shoulders with his fellow men. Neither does he fondly imagine that the most obscure brother can have nothing to teach him. "Ours is essentially a general practitioners' society," writes Dr. Bruce Low; but to regard "an ordinary G.P." as a member of a different and probably lower species is in the practice of our art as truly intelligent as to imagine that a battle can be fought successfully by an army composed entirely of generals. The general practitioner, besides being the liaison officer, the port of entry whereby the sick gain access to the treasuries of knowledge ready to be applied to their cure, necessarily possesses unlimited opportunities for observation. Chesterton remarked that one elephant with a trunk may mean nothing in particular, but when we notice that all elephants are born with trunks we suspect a conspiracy. In art a single mark may be meaningless, but the same mark oft repeated excites our interest and on closer scrutiny may reveal a pattern. An English village doctor observed that another and another and another of the milkmaids of the countryside did not get smallpox, and evolved a useful pattern from that observation. Let the medical society, therefore, as well as being a garden in which the rare plants of specialism may be propagated, be also a place where "the ordinary G.P." does not hesitate to speak of those things that by their mere iteration in his experience have forced themselves on his notice. Because his observations are simple and may seem to him commonplace, the practitioner should not refrain from voicing the conclusions to which they lead him, and no medical society should turn a deaf ear to what he has to say. If the sum of his observations be not wide enough to form the subject of a "paper," there is the valuable "communication" alluded to by Dr. Bruce Low, who wisely reminds us how often we are surprised to find that something we are familiar with and took for common knowledge is unknown to a fellow artist.

But if one should say he is no orator and cannot speak, let him be assured that every man has the ability to speak of that which interests him. Facility is born of practice. He must first think, then write his thoughts, then speak them, and we would add to what was said by a writer in these columns on a previous occasion, that not only must the reader of a paper speak out audibly, he must—when his observations are garnered, when the emergent facts are marshalled, when his paper is written—not merely read the paper, he must render and perform it as much as an actor performs a part or a musician renders a piece of music.

Few professions have the advantage possessed by the Army in the daily meeting place of the mess-room. If rank is not abandoned there, there is at least the reiterated opportunity for the small to observe at close quarters the marks and stigmata of greatness, and for the older to discern and direct the aims and potentialities of the younger. Our profession has no such opportunity, but its place is filled to some extent by medical societies such as that of Newcastle, with its exhibitions and discussions, its journal, of which the present issue is worthy of special comment, and by no means least, its opportunities for social meeting.

[1] THE LANCET, 1931, ii., 80.
[2] Newcastle Med. Jour., October, 1934.

## THE MONOCYTE AND MONOCYTIC LEUKOSIS

Doan's opinions on the monocyte[1] may not be generally acceptable, but they certainly deserve consideration—especially as he and his collaborators are largely responsible for the newer knowledge of this cell. He concludes that the monocyte of the blood is identical with the monocyte of the tissues and reflects directly and quantitatively the proliferative activity of these elements in the body as a whole; he distinguishes the monocyte of the blood and tissues—a derivative of mesenchymal reticular tissue—from the clasmatocyte which he regards as of endothelial origin. Circumstances which in pathological states result in monocytic hyperplasia are: first, the opportunity or need for phagocytosis of non-pyogenic bacteria or other particular matter (as in *Bacillus monocytogenes* infection of rabbits, and in

[1] Doan, C. A., and Wiseman, B. R.: Ann. Internal Med., 1934, viii., 383.

the monocytic reaction occurring in syphilis, typhoid, and undulant fever); and secondly, the presence of an excess of lipoidal substances occasioned either by disorders in the normal metabolism of fats or by the liberation in vivo, or by the parenteral introduction of foreign monocytogenic lipoids. For instance, it has been shown experimentally that the tuberculo-phosphatides will cause monocytic proliferation. Doan believes that the epithelioid cell of the tubercle is an altered phase in the life-cycle of the monocyte; consequently an absolute monocytosis in the blood in tuberculosis indicates the progressive formation of new tubercles in the tissues. Further, he claims that the cellular reactions in certain diseases known to involve disturbances in lipoid metabolism appear to be largely of monocytic origin—in Niemann-Pick's disease, in Gaucher's disease, and in Hand-Schüller-Christian's disease for instance. In the monocytes of monocytic leukæmia he has found vacuolar degeneration, which is possibly fatty, more frequently than in other leukæmias, which again suggests that some chemical stimulation affecting fats may be of ætiological significance. During a four-year period he has investigated 75 cases of leukæmia, of which less than 16 per cent. were examples of monocytic leukæmia, the diagnosis depending on hæmatological and pathological studies. Unlike Whitby and Christie, who last week described a case of monocytic leukæmia in our columns, Doan holds that there is no clinical syndrome pathognomonic of monocytic as distinct from myeloid or lymphatic leukæmia. In his own series every feature common to myeloid and lymphatic leukæmia was found in the monocytic form. The patients' ages varied from 4 to 70; seven were male, five female, and the known duration of the disease ranged from six weeks to four years. The principal sites of cellular proliferation were in lymphoid tissue, spleen, liver, and bone-marrow.

A study of the monocytic reaction by supravital technique in addition to ordinary methods is of value, Doan thinks, both for diagnosis and for the accurate and prompt assessment of therapeutic measures in a variety of conditions.

## THE NEUROTIC'S FRIEND

A CONSTRUCTIVE exposition,[1] by Dr. R. G. Gordon, of the attitude to be adopted towards a "neurotic" person by his family and friends, is the more valuable in that the advice tendered is applicable in almost any imaginable circumstance. Even if the label "a bundle of nerves"—a designation so adhesive that it can seldom be removed—has been stuck on without sufficient examination of the mental content, the wise handling here outlined will at any rate not intensify depressions or anxieties of psychotic origin. It may even reveal, by the lack of response shown to a consistent demonstration of uncritical friendliness, that indifference to the prospect of recovery which Dr. Gordon regards, with the liability to suicide, as one of the distinguishing characteristics of incipient psychosis as opposed to psychoneurosis. He notes in this connexion the decline of the once common belief that the same person may exhibit psycho-neurotic and psychotic reactions in succession. Opinion among experts is hardening on the fundamental difference between the neurotic and the potentially insane; the former, in a "mental breakdown", may develop hysteria or anxiety or obsessional neuroses, but these states will not progress in the direction most feared. This assurance will be no less welcome to the patient than to his friends and will help him by stigmatising as untrue as well as unwise any suggestion that unless he "pulls himself together" he will go mad. The implication throughout this monograph is that while elaborate psychotherapy should not be undertaken in the absence of exact diagnosis, since it may be inappropriate or even harmful, the patient's friend can hardly go wrong if he adopts a policy of which the essence is as follows: to refrain from obtruding advice; if his help is sought to listen patiently without interruption or criticism to a recital, however long and involved, of the patient's difficulties; to keep these confidences to himself; to encourage without exhortation or patronage; and to maintain a steady emotional attitude towards the sufferer. It is indeed the variation from alarm and despondency at the onset of symptoms to boredom and disapproval when these are pronounced to be functional that most depresses the patient and destroys his faith in himself, and thus retards his recovery.

Dr. Gordon in this "manual of first aid" makes no attempt to expound behaviour in the language of psycho-analysis, individual psychology, or analytical psychology, preferring to explain the crises which may determine a neurosis in everyday terms within common experience. It follows that to whatever school of thought the family medical adviser may belong, he will find that his efforts to restore harmony to a disorganised home will be more speedily successful if he persuades the patient's friends to attack the situation on the simple and sane lines here laid down.

## GOITRE AND IODINE DEFICIENCY

IN some parts of New Zealand at least every third school-child has a goitre, and for the last ten years workers from the medical school of Otago University have been following every known clue to its origin. Up to 1928 there were at least half a dozen rival theories—e.g., fæcal contamination of water, radio-activity of water, salts dissolved in drinking water, general diet, geological formation, iodine deficiency in diet—each with their protagonists. But in that year an exhaustive survey of the whole country by Prof. C. E. Hercus, Prof. W. N. Benson, and Mr. C. L. Carter—respectively bacteriologist, geologist, and chemist—led to the provisional conclusion [1] that the incidence of goitre in New Zealand was inversely proportional to the amount of iodine in the soil. A bulletin published in that year by the official departments of health and scientific research embodied the findings of this survey, accepting in general the inverse relationship between goitre and soil iodine. There were then admittedly some exceptions; for instance, while South Taranaki soils were found to contain four times the proportion of iodine in Thames soils, the incidence of goitre was rather greater in the former than the latter district, and New Plymouth, with about 13 times as much iodine as Thames, had approximately the same incidence of goitre. A further inquiry was undertaken by the two officers who had carried out the original investigation, and their report [2] has now appeared. Three districts were selected: (1) the anomalous Thames; (2) Palmerston North, in which soil iodine had been found to be low

[1] The Neurotic and His Friends. By R. G. Gordon, M.D., D.Sc., F.R.C.P. Edin., physician, Royal United Hospital, Bath: associate physician, Institute of Medical Psychology. London: Methuen and Co., Ltd. 1934. Pp. 87. 2s. 6d. [Methuen's Monographs on Philosophy and Psychology: General editor, G. C. Field, M.A., B.Sc.]

[1] THE LANCET, 1928, ii., 768.

[2] New Zealand Department of Scientific and Industrial Research, and Department of Health. Bulletin No. 45. Goitre in School-children. By Dr. R. A. Shore and Mr. R. L. Andrew. Wellington: Government Printer. 1934. 1s. 6d.

and goitre incidence high; and (3) New Plymouth (including part of South Taranaki) in which iodine was high and goitre low. The total number of children examined was 4012 boys and 3782 girls, and the goitres were classified as "A" or "incipient" and "B" or "visible." Later a fourth district—Gisborne—was added. This area had previously shown a high incidence of goitre, but most of the cases fell into the incipient class, and it was desired to find out whether there was any alteration in the proportion of "A" and "B" goitre. Gisborne, however, alone of the four areas under survey, showed a reduction in the incidence of goitre among its school population. Each of the other three areas exhibited a deplorable increase, and New Plymouth, which had come out of the previous investigation nearly goitre-free, gave the alarming figures of 82 per cent. goitre in boys and 88 per cent. in girls. Thames had risen from 8 per cent. boys and 9 per cent. girls suffering from goitre to 23 and 31 per cent., and Palmerston North from 35 per cent. boys and 39 per cent. girls to 67 and 73 per cent. respectively. One outstanding variation in the result of the two surveys is that, whereas in 1928 the incidence of goitre among girls began to decline after the age of 13, in the later group the increase continued up to 15 years. Differences in iodine intake in varying districts being mainly due to locally produced foodstuffs, the investigation was specially directed to vegetables, milk, and eggs, from which it appeared that the intake of iodine would be nearly twice as high at New Plymouth as in Palmerston North or Thames. The result of the second survey is to reverse the findings of the first. The investigators were the same, the material was similar, and no noticeable change had occurred in the circumstances in which the children were living; yet, whereas the previous finding was high intake of iodine associated with low incidence of goitre and vice versa, the opposite was true of the second group examined. No explanation is at present available of the enormous increase of goitre in the school-children of Taranaki. The whole subject of the importance of iodine in relation to the disease is shrouded in perplexity.

## POLICE LABORATORIES

RECENT announcements would suggest that it is the intention of the authorities at Scotland Yard and the Home Office to establish, at various police-training centres throughout the country, laboratories where instruction can be given to students in the scientific methods of crime detection. Dr. Norman Burgess, formerly Anderson demonstrator of clinical chemistry at Guy's Hospital, is in charge of the Criminal Investigation Research Laboratory at Bristol; Dr. James Davidson, senior pathologist to the Edinburgh Royal Infirmary, has been appointed director of the laboratory at the Metropolitan Police College at Hendon; and it has been suggested that similar centres should be established at Nottingham, Birmingham, Manchester, and Leeds. This system would then be on a par with that in certain continental countries where each police-training centre has its own laboratory. Comparisons between the police system of this country and those on the continent have for some time past resulted in criticism of the laboratory facilities here as both inadequate and lacking in modern methods and equipment. While the new departure may be intended to meet this criticism, it should not be admitted too readily that the results attained under our present system suffer by comparison with those obtained abroad. Some of the methods in use on the continent have been tried in this country and found wanting. Training in scientific method is another matter. The proposed centres of instruction will be of untold benefit if they make it less likely for valuable evidence to be missed by police officers, especially if closer coöperation is ensured between the authorities in different parts of the country. One of the main functions of the director of the laboratory at the Metropolitan Police College is to be that of "assisting in the investigation of criminal cases." Hitherto investigation has been left in the hands of a few experts in their own branch of science—toxicology, for instance, morbid anatomy, metallurgy, or forensic ballistics. Their very independence has been a characteristic of the justice meted out in the criminal courts of this country. But even experts can only be in one place at a time, and their services are often in demand in several places. The training of potential police leaders is getting more intensive and scientific; it is their job to find out if crime has been committed, and if so, by whom. The new scientific knowledge, e.g., the identity of a particular bullet with a particular gun-barrel track, is to be made available in many centres instead of concentrated at Scotland Yard. But if policemen everywhere are to be more skilled and prompt in using technical resources in detection, expert witnesses will still be wanted as much as ever to get the results into a jury's head.

## AN ESSAY ON BAHNUNG

IN the John Mallett Purser lecture[1] for 1934, delivered at Trinity College, Dublin, Prof. Ariëns Kappers of Amsterdam presents an old problem under a neurological guise—the question as to which came first, the hen or the egg. The cell groups or reflex centres of the nervous system develop at different rates and at different times, many of them altering their position in the central neuraxis and some migrating outside it. Axones grow out from these cells and push their way, often for long distances, before establishing contact with other cell stations in the brain or cord or with receptor or effector organs outside. A complex anatomical machine is built up long before it can be applied to any useful end, its various processes of construction being related to one another only in so far as they combine to provide a physiologically functioning end-result. In the earlier state of our knowledge these developments appeared to demand a purely teleological explanation—that is to say, one implying purpose. Prof. Kappers set himself to examine whether these processes may not be interrelated in other ways. It is known, for example, that the development of certain ganglia in the central nervous system depends largely upon the number of nerve-fibres running to them, and that the direction taken by a developing nerve-fibre is determined chiefly by the state of the remote ganglion to which the fibre will make its way. Thus the development of the corresponding centre in the brain is prevented by the removal of an eye, and is greatly increased in complexity by grafting an extra eye—in either case at a stage of fœtal existence when none of these structures can be normally stimulated. Two things, Prof. Kappers believes, guide this "mnemic predecession" as he calls it. First the attraction of growing fibres by existing centres, secondly (and more important) the growth in complexity of centres under the influence of converging fibre tracts. He considers very fully how these effects may be produced, and in support of his suggestion that the frequency and

[1] Irish Jour. Med. Sci., September, 1934, p. 495.

rate of conduction of nerve impulses can exercise an effect upon the centres to which they run, he quotes Sherrington's classical observations on reflex facilitation, or *Bahnung*, as it is called on the continent. The choice as to which of two available responses shall be made to a stimulus which may elicit either—and hence the choice as to which of the two reflex centres mediating these responses shall receive the afferent impulses originating from the stimulus—depends upon the fact that preceding stimuli may have elicited one of these responses, and thus have facilitated its reproduction by the "induction" of the impulses of following stimuli towards the corresponding reflex centre. This explains why in a dog when a scratch response to stimulation is in train, an added stimulus, which by reason of its position would not alone have elicited a response, greatly increases the existing response. And why in a cat the direction of the movement of the tail when it is touched depends on its position when touched. To these classical examples of *Bahnung* Prof. Kappers adds what he claims to be another no less striking example. In insects which move towards the light this photokinetic response depends upon the activity not only of the facet eyes but also of the ocellæ. Thus when both ocellæ are covered an insect moves invariably towards the nearer of two equally brilliant lights. If only one ocella is uncovered the insect will move towards the light on that side—even though it be the more distant light. Since with both eyes covered no photokinetic response at all is observed, although both ocellæ are uncovered, he assumes that the ocellæ act not by adding the effects of their own photokinetic response to that of the eye, but each by facilitating one of the alternative motor centres and hence inducing the afferent impulses from both eyes towards that centre. Prof. Kappers then adapts the principle underlying these observations to his present context by suggesting that in development the centres that are earliest stimulated will remain predominant because all later stimuli will tend to be induced along the same path towards them. He claims that even without having previously received any incoming stimuli all "proliferating centres" determine the growth of axones in their own direction by acting as previously stimulated cell groups. And he assumes that the same factor or factors which determine the direction of flow of the afferent nervous impulses will determine also the direction of growth of incoming neurones.

## IRON IN INFANCY

LITTLE is known about the metabolism of iron, either in man or animals, and by investigating the intake and output of iron in six normal infants H. W. Josephs[1] has made a stimulating contribution to our knowledge. Four of them were studied from the second to the twelfth week, one from the sixth week to the sixth month, and one from the second week to the sixth month. It was found that in the first two months of life there tended to be a negative iron balance, which, however, did not cause a loss of more than a few milligrammes. The balance then became positive and remained so as long as the observations were carried on. Although the period of negative balance corresponded in general to the period of falling hæmoglobin there was no clear relationship between the reduction of total hæmoglobin and the negative iron balance. The positive balance corresponded to the time when the hæmoglobin was rising; but again there was no relationship between the body's gain in iron and the increase in total hæmoglobin, the positive balance covering only a small proportion of the total needs. There is therefore no close relationship between iron excretion and hæmoglobin loss or gain. From somewhat elaborate calculations Josephs concludes that it is impossible to account for an iron-deficiency anæmia in the average child on the basis of a relative absence of stores at birth and a normally rapid growth. It is necessary to look for other factors that actually diminish the total amount of iron in the body or increase the relative growth. Prematurity is one such factor, largely because of the relatively more rapid gain in weight. A second is infection. One child during observation showed a greater loss of iron during a slight cold than either before or after. Further calculation indicates that an exclusive milk diet cannot cause any great degree of anæmia on the basis of its low iron content alone; other factors causing a disturbance of iron metabolism must be present. Hawksley, Lightwood, and Bailey[2] elsewhere suggest that one of these factors may be hypochlorhydria or achlorhydria, since in 12 out of 13 patients ranging from eight months to ten years in age, with an iron-deficiency anæmia, they found achlorhydria following an alcohol test-meal. In some of the cases in which the observations were repeated using histamine the same results were obtained. Clearly, until we know more of the factors influencing the metabolism of iron, we cannot hope to understand the mechanism of anæmias due to deficiency of it.

[1] Josephs, H. W.: Bull. Johns Hopkins Hosp., 1934, lv., 259.

## THE NERVOUS CONTROL OF SWEATING

THE sweat glands are interesting in that they respond to parasympathomimetic drugs, although their innervation is actually from the spinal sympathetic. Recent work, already well known, has shown that in the autonomic system as a whole there are two ways by which a nerve impulse may be transmitted from one neurone to the next, or from a neurone to an organ which it innervates. The first method is the liberation of acetylcholine at the nerve-ending, the second is the liberation of an adrenaline-like substance. All pre-ganglionic fibres pass on their impulses through the mediation of acetylcholine, but post-ganglionic nerves may use either substance. Most terminal parasympathetic fibres use acetylcholine, and most sympathetic fibres adrenaline or its equivalent. The rule is only a general one, however, and some sympathetic fibres are "cholinergic," some parasympathetic fibres "adrenergic." W. C. Wilson,[3] of Edinburgh, points out that though the sweat glands of the cat's paw are supplied by sympathetic cholinergic fibres there is some evidence, mostly based on the mode of action of pilocarpine, that the story is not so simple in man. By careful study of the sudorific activity of pilocarpine after simple section, or degeneration of motor, sensory, and autonomic nerves in man, he comes to the conclusion that there is no need to postulate any double or unusual innervation. The drug acts directly on the sweat glands themselves, not on nerve-endings, and presents many other similarities to acetylcholine.

Uprus, Gaylor, and Carmichael[4] also eschew complicated theories in their interpretation of a case in which flushing and sweating occurred in the

[2] Hawksley, J. C., Lightwood, R., and Bailey, U. M.: Arch. Dis. Childhood, December, 1934, p. 359.
[3] Wilson, W. C.: Brain, 1934 lvii., 422.
[4] Uprus, V., Gaylor, J. B., and Carmichael, E. A.: Ibid., 1934, lvii., 443.

right submental region upon eating; this was the result of excision of neck glands in childhood. The case gave unusual facilities for detailed observation, which led to the conclusion that the symptoms were not due to any accentuation, spread, release, or other modification of a normal pre-existing reflex, but probably to the peripheral regeneration of fibres of the chorda tympani along foreign vasodilator paths. This would result in flushing and sweating in the area of supply when the chorda tympani was active, instead of during activity of the original, but now displaced, vasodilator fibres with normal central connexions. A similar explanation is suggested for two analogous syndromes—namely, flushing and sweating over the distribution of the auriculo-temporal nerve during eating, and lacrymation ("crocodile tears") from the same stimulus.

## DENTAL INFECTION OF THE MAXILLARY ANTRUM

LYING in the borderland between dentistry and rhinology, the pathology and treatment of dental infection of the antrum are apt to get less detailed attention in the text-books than they deserve; so that the paper[1] read by Mr. Myles Formby before the University College Hospital dental students' society is particularly welcome. Authorities differ widely about the proportion of cases in which the antrum is infected from the teeth; and it even appears that sometimes the teeth are infected by suppuration in the maxillary sinus; but dental infection is, at any rate, an established and important cause of antral disease. There are four possible routes by which it may reach the antrum: (1) Direct introduction by rupture of a perisinus or alveolar abscess, by a fracture of the floor of the antrum, or by a root pushed up into the cavity. (2) Spread by continuity, the commonest type, in which the usual sequence of events is dental caries, apical infection, submucous infection, area of diseased antral mucosa, empyema of the antrum. Since such cases not infrequently become manifest during an acute rhinitis, the teeth may escape suspicion and, if treated by the rhinologist by intranasal antrostomy, the suppuration will continue as long as the dental focus of infection remains. On the other hand, if the dentist discovers the apical abscess and extracts the tooth, an acute exacerbation of the latent antral disease may be set up, and the patient blames the dentist. (3) Infection through the blood and lymph streams, though mentioned in most text-books and undoubtedly a possibility, is in Mr. Formby's opinion very improbable. (4) Spread on the surface of the mucous membranes, a route which he finds is not sufficiently well recognised; by this he means infection of the nasopharynx and nose by the multitude of organisms present in the mouths of patients with caries or pyorrhœa. Clinical facts lend some support to this theory, for many patients suffering from postnasal catarrh, obstruction, or frequent persistent colds, are found to have oral infection and to be completely relieved by attention to the teeth.

In considering treatment Mr. Formby makes some valuable remarks. When, after an extraction, an opening into the antrum is suspected, care must be taken, he says, to remove all diseased tissue and to leave the cavity to drain freely, but damage to the depths of the alveolus should be avoided; filling of the cavity with bismuth paste may be used to prevent the entry of particles from the mouth while allowing free escape of discharge. The antrum is transilluminated, and washed out within 24 or 48 hours through the nose if found to be dark. If, on extraction of the tooth, pus escapes freely from the alveolus, the socket is carefully syringed; should fluid escape into the nose, a fistula is present, and there is an empyema of the antrum. In such cases, and whenever pus is found on washing out the antrum, intranasal drainage should be established. Plugging the dental fistula is strongly condemned, for this prevents its closure. In cases where the antrum is apparently healthy, and at extraction the floor of the antrum is fractured, the alveolus is cleansed with a strong antiseptic such as spirit or 1 in 20 carbolic, and when possible the fistula is closed by suture of the alveolar mucoperiosteum. The antrum should be transilluminated; if dark, it probably contains blood and should be washed out to lessen the probability of subsequent infection; if clean, it is likely to escape, but should be watched. If the fistula cannot be closed by suture, it is best left widely open. The most difficult cases are those in which a portion of tooth disappears into the antrum; it may sometimes be recovered at once by means of a small blunt scoop or a bent probe, or by packing the antrum through the fistula, when it may be caught in the folds of gauze and so removed; the fistula may be enlarged for the purpose, and subsequently sutured, provided that the degree of infection is slight. If the tooth is not recovered, the antrum must be opened through the canine fossa, with a free opening into the nose for drainage. A skiagram must first be taken, and it is by no means always easy to find the fragment, which may be hidden in a recess of the irregular cavity or lie under the mucous membrane.

There remains the question of the treatment of an established fistula. If it remains patent for more than a month, it will become lined by epithelium, and it is for this reason that all forms of packing should be avoided. The first essential is to establish free intranasal drainage, and at the same time the lining of the fistula should be excised together with any adjacent diseased bone. It may close after this procedure, but when it is large or has existed for more than a few weeks a plastic operation is usually required.

[1] Brit. Dent. Jour., 1934, lvii., 582.

## METHYLATED SPIRIT DRINKING

NEARLY a year ago the House of Commons debated in a friendly way the second reading of a Bill moved by Miss Horsbrugh which would limit the retailing of methylated spirit to a list of persons certified by the local authority to be suitable. The Bill proposed further that the vessel containing the spirit should be labelled and the seller required to enter in a register the purpose for which the spirit was to be used. Miss Horsbrugh felt that a provision of this kind would result in warning a great many people for the first time how harmful it would be to drink methylated spirit. Sir E. Graham-Little thought the objects of the Bill might be attained more easily than in the way suggested, and Mr. Hacking for the Home Office said he had grave doubts about the effectiveness of its provisions. In 1932, the latest complete statistical year, 596 persons were convicted for drunkenness ascribed to methylated spirit drinking. These convictions, he said, represented only 2 per cent. of the convictions for drunkenness and 0·001 per cent. of the total population. Miss Horsbrugh's motion when put to the vote was carried by 48 to 28, a majority insufficient for an affirmative decision. Dr. Percy Turner, medical officer to the Salvation Army, in an address to the Society for the Study of

Inebriety on Jan. 8th, referred to the failure of the legislature to restrict the sale of methylated spirit and quoted reports from various Salvation Army shelters to show that the habit of methylated spirit drinking was widespread. Clearly, he said, the spirit was much too easily obtained. Sir William Willcox had drawn attention to the evils arising from drinking impure forms of alcohol; these included mental deterioration leading to insanity, and blindness. In 1926 2000 deaths were attributed to the drinking of methylated spirit in the United States. It was common knowledge there that 10 cents worth of "smoke"—so called because crude wood-alcohol becomes cloudy on the addition of water—sufficed to cause drunkenness. In Scotland about a thousand cases of drunkenness a year, he said, were attributed to methylated spirit drinking. This was presumably much within the fact, since the police were not allowed to report drunkenness as due to methylated spirit unless the bottle was found on the person. A serious phase of the evil was the purchase of a cheap port or other wine and the addition of methylated spirit to impart the desired kick. If the drinker kept within doors no conviction could follow. The ecstatic feeling soon wore off, leaving a deep mental depression, which the victim sought to dissipate by further indulgence, resulting in a progressive deterioration. It seemed to be agreed, said Dr. Turner, that after a methylated spirit carouse overnight the drinking of water on the following morning produced a further attack of drunkenness. This he attributed to the residue of crude spirit in the stomach being rendered absorbable on dilution with the water. In Glasgow the drinking of surgical spirit was another phase of the drug habit; its sale for this purpose was reported to be on the increase. Dr. Turner suggested that less wood naphtha should be used for denaturing spirit and something added like crude pyridin to produce vomiting after drinking. Dr. J. D. Rolleston recalled Dr. F. S. D. Hogg's suggestion made in our own columns to add half a grain of tartar emetic to every ounce of methylated spirit. Dr. A. E. Carver noted the case with which propyl alcohol could be obtained as perfume. On a sixpenny bottle from a cheap store a person could get drunk several times.

## A PITFALL IN DIAGNOSIS

THE medical student is laboriously trained not to attribute symptoms to several different causes if a single disease can be found to explain them all. This training is very necessary, for to beginners (and patients) the unhealthy body often seems to be a museum of unrelated illnesses. Nevertheless it may easily lead one into the opposite error. Having once discovered an organic disorder it is tempting to make it responsible for all the associated complaints, and this may have serious consequences where, as so often, it attaches the patient's functional nervous symptoms to an organic lesion that cannot be mended. Apart from their effect on the mind, mistakes of this kind are liable also to lead to inappropriate treatment; for example a person with a mild perfectly compensated mitral stenosis may be taken off work or even put to bed for weeks should he complain of dizziness, a pain under the left breast, or any one of the many symptoms associated with a lowered condition of general health. It is undoubtedly true, as T. F. Cotton [1] has said, that "in a patient with signs of structural disease of the heart there are few symptoms that cannot arise from other causes than disease of the cardiovascular system." In his Bancroft lecture at Brisbane Dr. Bickerton Blackburn[2] refers especially to the difference in the picture coronary occlusion may present when seen in a patient of a phlegmatic and unemotional habit and in one who is nervous or irritable. Whereas placid people are little troubled by pain after the first few days, and rarely complain of it after recovery, those who are nervous or irritable have recurrent pains and vasomotor phenomena, brought on by excitement, transitory flatulence or "even the late arrival of the doctor," which may cause anxiety and fear that the thrombosis is spreading. In conclusion he says "you will at least agree that the interpretation of the nervous relationship of disorders of the heart is one of the most difficult and at the same time most interesting of the problems with which a physician is confronted," and this is a lesson emphasised, incidentally, in the valuable case-record which Dr. J. H. Williams presents on p. 147. Looking at the problem from a different side it is clear that the sensory and nervous system can control or modify the symptoms which arise directly from an organic lesion. An excellent example of this has recently been given in our own columns by letters in which two medical men, sufferers from coronary thrombosis, related their after-experiences.[3] Among other comments one remarks that "sunshine and all that it brings make pain disappear," and goes on to say that in Switzerland he can ski and skate quite comfortably but that an expedition on a dull day, where he had to be at a certain point at a certain time, brought on the pain. He also records that the fear of pain coming on is likely to evoke it. The other practitioner wrote: "I can walk miles, but . . . an annoyance, or a competitive game . . . or feeling *compelled* to do anything, bring on pain at once."

What is true of cardiac conditions is true also of other organic diseases, but it is probably in cardiovascular affections that misapprehensions are most likely to have a disastrous influence on the patient, his family, and his friends.

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IN spite of the economic depression New York City is able to report the lowest general death-rate in its history—10·15 per 1000 of population. The report of the health commissioner. Dr. John L. Rice, is generally encouraging: typhoid fever showed a further decline; there were fewer cases of diphtheria than ever before, though the increased case-fatality shows that the type is more virulent; the number of deaths from tuberculosis, as well as the death-rate, continues to diminish, and the infant mortality-rate, at 52·2 per 1000 births, is only a little higher than in 1932, the record year. Suicide and malnutrition have both been decreasing for two years—perhaps because of more efficient measures of relief. Dr. Rice refers to Brodie's method of vaccination against poliomyelitis [4] "which seems to offer an effective immunising agent." He also points out that the total of 1604 cases of diphtheria compares very favourably with the average of 10,685 per annum in the decade 1920–29 before immunisation began.

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[1] Brit. Med. Jour., 1924, i., 307.

[2] Med. Jour. Australia, 1934, i., 829.
[3] THE LANCET, 1934, ii., 331 and 385.
[4] See THE LANCET, 1934, ii., 610.

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EAST HAM CLINIC.—A new clinic for maternity and child welfare work has been built at East Ham at a cost of about £5000.

# PROGNOSIS

*A Series of Signed Articles contributed by invitation*

## XXXVI.—PROGNOSIS OF DIABETES MELLITUS IN ADULTS

THE prognosis in a case of diabetes mellitus depends on a number of factors, notably :—

1. The severity of initial attack, the response to treatment, and the time which elapses before treatment is started.
2. The degree of intelligence and coöperation of the patient and his attendants.
3. The ease with which blood-sugar can be controlled.
4. The incidence of other diseases and the skill with which the dose of insulin is adjusted to meet the changed conditions.

The cause of diabetes is not yet known, but it is certain that a patient with this disease produces an amount of insulin insufficient for his requirements. It is not, however, established that this defective secretion is due in every case to a lesion of the beta cells of the islands of Langerhans. It is possible that the supply of insulin—i.e., the amount secreted—may be normal but that for some reason the demand is excessive.

### SEVERITY OF INITIAL ATTACK AND RESPONSE TO TREATMENT

It is a curious fact that in many young adults the prognosis appears to vary inversely with the severity of the initial symptoms, though this is by no means an invariable guide. In some young adults the initial metabolic disturbance is severe and the patient complains of great thirst and loss of weight. Many of these acute cases if treated early with diet and insulin do very well indeed, and the insulin can eventually either be greatly reduced or abandoned altogether. In others, where almost the only symptom is glycosuria, perhaps discovered incidentally, the initial damage is apparently very slight, and insulin is either not needed at all or only in a small amount which is discontinued very soon. The prognosis seems good but it may not be so, for within a few months glycosuria may return and insulin may have to be restarted with continually increasing dosage. It is well to wait until a year has elapsed before giving a prognosis, since the evidence of a progressive or stationary lesion will then be available. The contrast between the two types is not so clear in elderly people, but it can often be detected.

### THE PATIENT'S INTELLIGENCE AND COÖPERATION

The degree of intelligence which the patient possesses or is prepared to give to the essential study of the disease and its treatment plays a great part in determining the progress of the disease. Some intellectual people are very tiresome in this respect, as they profess to have neither the time nor the inclination to think about the petty details of their diet. At the other end of the scale we have patients who are unable even after considerable effort to understand the simple rules for diet, insulin, and urine testing. Another group, although they appreciate the necessity of considering their diet, are unable to resist the temptation of adding carbohydrate to it. They admit that the total carbohydrate allowed for the day or meal is adequate but any sudden temptation—e.g., sweet cakes at a tea table—is too much for them. If these irregularities occur often the disease tends to progress. The best chance of increasing the sugar tolerance lies in keeping the carbohydrate content and the timing of meals, and also the timing of insulin injection, as constant as possible. Occasional variations do little or no harm but repeated changes are undesirable. Once the diagnosis has been established by blood-sugar estimation it is unnecessary for such tests to be made frequently, but it is important for the patient to test his urine regularly for sugar. Some patients seem to have psychological difficulties in doing this. Among the various reasons offered for neglect, none of which seem adequate to the physician, are: (1) the time taken in doing it ; (2) the fear of finding sugar ; (3) the irritation of being constantly reminded that they have diabetes ; and (4) the constant absence of any sugar. It is lamentable how often patients with a mild form of the disease return after some months in a much worse condition. They usually admit that they first gave up testing the urine for one reason or other, and then added more food. Weeks or months may elapse after glycosuria has returned before the patient has any symptoms.

### CONTROL OF BLOOD-SUGAR

A very important point in prognosis is the ease with which the blood-sugar can be controlled and kept within normal limits. If this can be achieved easily without attacks of hypoglycæmia the progress is much better. In the great majority of cases this is easily accomplished, but the ideal may have to be abandoned in some because the patient may develop severe hypoglycæmia at midday or during the night. It is often possible to prevent this condition by giving "buffer" meals of 10–15 g. of carbohydrate in the middle of the morning or on going to bed before the hypoglycæmic attack usually develops. If this régime fails to prevent the hypoglycæmic attack some glycosuria must be permitted, but the chance of decreasing the dose of insulin is reduced.

### THE EFFECT OF COINCIDENT DISEASE

The development of other diseases is always serious, for it increases the insulin requirements. A very acute illness—e.g., appendicitis—may cause the onset of coma, while even more trivial ailments like a "cold in the head," influenza, boils, and minor forms of sepsis may cause glycosuria and necessitate an increase of 2 or 4 units of insulin. Tuberculosis is always a serious complication as it requires a high caloric diet and larger doses of insulin. The prognosis is immensely improved if these complications are treated early in the appropriate manner, and especially if the dose of insulin is at once increased. Coma should never develop in any patient who is being treated for another disease, as it is easily prevented by increasing the dose of insulin to a sufficient amount. Pregnancy and its complications may make the diabetic condition temporarily worse, but as a rule the evil effects pass away in a few months after parturition provided that the dosage of insulin is carefully controlled.

Two grave complications are liable to occur in the elderly diabetic : (1) cataract and diabetic retinitis, (2) atheroma and gangrene of the extremities. It is generally believed that eye complications are more likely to increase and progress if the diabetic condition

is not kept well under control, but both conditions unfortunately occur even in patients with mild and well-controlled diabetes. The presence of atheroma in adults after the age of 30 has caused considerable concern. The modern system of allowing increased carbohydrate and the reducing of the fat in the diet is considered likely to decrease the frequency of the occurrence, provided that the diabetic condition is carefully controlled with insulin. The development of gangrene always greatly aggravates the diabetic condition and very large amounts of insulin may be required. When the gangrenous area has healed or the limb has been amputated, the dose of insulin can be greatly reduced and sometimes given up altogether.

CONCLUSION

The prognosis in the case of the intelligent and well-treated diabetic patient is good, and patients nowadays always feel well however much insulin they may require. Young children usually grow and develop quite normally though puberty may be a little delayed. They are able to attend either day or boarding schools, and suffer very few disabilities. Older people feel fit and are able as a rule to return to their normal occupations provided that these occupations do not involve hard manual work.

GEORGE GRAHAM, M.D., F.R.C.P. Lond.,
Physician, St. Bartholomew's Hospital.

# SPECIAL ARTICLES

## THE PHYSICAL FITNESS OF RECIDIVISTS ASSESSED BY VITAL CAPACITY *

BY F. E. E. SCHNEIDER, M.D. Lond., D.P.M.
MEDICAL SUPERINTENDENT, RAMPTON STATE INSTITUTION

THE theory of Lombroso has been discredited; we no longer believe that the criminal is an anthropological monster, with stigmata which distinguish him from the rest of mankind. But it still remains to be shown what factors influence a man's development, so that he becomes by habit a law-breaker, and to that extent different from the majority of his fellows.

In his monumental "Statistical Study," Goring stated that the English convict was "markedly differentiated by defective physique—as measured by stature and body-weight; and by defective mental capacity—as measured by general intelligence." The investigation about to be described was undertaken whilst I was on the medical staff at H.M. Prison, Pentonville, with a view to determining whether the physical fitness of the recidivist showed any marked deviation from the normal. It was felt that a functional measurement such as the vital capacity, which varies with the health of the individual, would indicate whether his physical fitness, and therefore his available energy, was noticeably different from that of his more respectable brethren.

Martin Flack, working amongst Royal Air Force officers during the late war, found that the vital capacity corresponded directly with flying fitness. Georges Dreyer has shown the value of vital capacity as an index of health and that the vital capacity can be used to give a prognosis in pulmonary tuberculosis. He has compiled also tables of vital capacity from every class of citizen, and it was with these tables, set out in his "Assessment of Physical Fitness," that the figures obtained at Pentonville were compared.

When it is remembered that mental health and bodily health are interdependent, these measurements take on an added significance, especially if it is accepted that a certain proportion of prisoners belong to the "social problem," or mentally subnormal, group.

The population of Pentonville contained no first offenders and no prisoners under 25 years of age. They were thus an ideal body of men for exhibiting the criminal diathesis.

The method described by Dreyer was followed closely.

The measurements taken were: (1) length of trunk, (2) circumference of chest, (3) body-weight, and (4) vital capacity. For the last-mentioned the spirometer made by Boulitte, of Paris, was employed, for the sake of uniformity in comparing with Dreyer's tables. It is a simple instrument of the gas-meter type, into which the subject empties his lungs after a full breath, and this air passes over a system of fans, and the volume is recorded on a dial. The subject's trade or occupation is important, and places him in Class A, B, or C, according to whether his life is active or sedentary; the classes are typified by Dreyer as (*a*) athletes, (*b*) professional men, (*c*) tailors, clerks, &c., respectively. The age was found by Dreyer to be of little importance up to 50, and it was neglected.

The comparison with the tables was effected in the following way. The weight according to length of trunk and the weight according to circumference of chest (as shown in the appropriate tables) were added together and divided by two; the result was compared with the weight of the prisoner, and if the difference was not greater than 10 per cent., the latter was taken as a normal weight. Then the prisoner's vital capacity was compared with another table, which showed whether it placed him in Class A, B, or C, according to his body-weight. If his vital capacity was more than 10 per cent. below the normal for his mode of life, he was to be regarded as having inferior health at the time of the examination. If he were found to be too heavy or too light, adjustment was made by reference to still other tables which showed the relation of vital capacity to trunk-length and to chest circumference.

Upwards of 1500 prisoners were examined and assessed in this way during 1931 and part of 1932. In the first place the observations were made only on reception, but later on an attempt was made to take readings both on reception and discharge, so that the effect of imprisonment upon physical health might be gauged. Double sets of readings were obtained in 600 cases. Examples will serve to show how the figures are dealt with.

No. 4785, a barman, convicted of indecency. Trunk-length 34½ in.; chest 35¾ in.; weight 145 lb.; vital capacity on reception 3330 c.cm., on discharge two months later 3450 c.cm. The tables show that the weight for a trunk of 34½ in. is 127·9 lb., and for a chest of 35¾ in. circumference is 164·9 lb.; adding these and dividing by two we get 146·4 lb., which is not more than 10 per cent. greater than 145 lb., the observed weight of the subject. The tables of vital capacity for weight show a vital capacity of 3644 c.cm. for 145 lb. in Class C, to which this prisoner belonged, so that he was 114 c.cm. below the normal, which is less than 10 per cent. After two months' imprisonment his vital capacity had risen by 120 c.cm.

No. 4793, a tailor, convicted of stealing. Trunk-length 34 in.; chest 34½ in.; weight 133 lb.; vital capacity 3010 c.cm.; normal weight 137·5 lb.; vital capacity in Class C for 133 lb. is 3424 c.cm. He was thus 414 c.cm. (more than 10 per cent.) below the normal.

* Published with the consent of H.M. Prison Commissioners, but not necessarily representing their views.

No. 4789, a tailor, convicted of larceny. Trunk-length 32 in.; chest 32 in.; weight 130 lb.; vital capacity 2570 c.cm. For a trunk of 32 in. the vital capacity should be 2865 c.cm.; for a chest circumference of 32 in. the vital capacity should be 3213 c.cm. The vital capacity in Class C for weight of 130 lb. should be 3369 c.cm. His vital capacity was therefore more than 10 per cent. less than the lowest figure.

In this way it was found that out of 1500 prisoners, 1386 (or 92·4 per cent.) had a vital capacity less than normal by not more than 10 per cent.; 54 (3·6 per cent.) had a vital capacity less than normal by more than 10 per cent.; and in 60 (or 4 per cent.) the vital capacity was greater or equal to the normal. It must be pointed out that sick prisoners admitted into hospital on reception were not included in this investigation, so that serious physical illness does not obscure the issue.

Six hundred prisoners were subjected to this examination on discharge as well as on reception. Of these, 362 (or 60·3 per cent.) showed an increase of vital capacity after serving their sentences; 180 (or 30 per cent.) showed a decrease; and 58 (or 9·6 per cent.) were unchanged. It happened that of the group whose vital capacity increased during imprisonment, 18 had a vital capacity on reception that was normal or greater than normal; the remainder (95 per cent.) improved, but only 2 reached a normal figure.

The conclusions to be drawn from the investigation (so far as its conditions are accepted) are: (1) that the vitality or health of the average criminal recidivist is not much below that of other men; (2) that his health improves in favourable surroundings (which implies that his surroundings were not favourable when he committed the offence); and (3) that imprisonment has a beneficial effect on his health.

## MEDICINE AND THE LAW

### The Weymouth Inquest

THE Weymouth inquest upon the death of Jefferys Charles Allen, the 86-year-old magistrate, found dead on Nov. 18th with his head in a sitting-room fire, was interesting as an instance where a coroner allowed legal practitioners the rare privilege of addressing the jury. The proceedings thus approximated to those of a criminal trial where a defendant is accused of a definite charge. Major Symes, the Weymouth coroner, was fully entitled to allow the case to proceed as it did. The circumstances of the death by burning required investigation in themselves. In addition Mrs. Jackson, who acted as secretary-companion to Mr. Allen, benefited by a codicil, executed three weeks earlier, whereby he left her £8000, apparently the whole of his money. This fact, and certain evidence of witnesses unfavourable to Mrs. Jackson, raised suspicions into which it was the coroner's duty to inquire, though it by no means follows that the prospective inheritance of £8000 from an 86-year-old testator must make the beneficiary so impatient as to murder him. The Director of Public Prosecutions made no appearance; his intervention at the inquest might have conveyed an impression unfair to Mrs. Jackson. No parallel proceedings before magistrates caused an adjournment of the inquest. As Major Symes observed, sometimes the coroner and the police have no doubt that murder has been committed, but are uncertain as to the possible culprit; here there was uncertainty as to whether there had been a murder, but there was little doubt as to the person on whom, if murder was established, suspicion would fall. The chief constable of Dorset instructed counsel to appear for the police at the inquest, and Mr. W. Maitland Walker (who appeared in this capacity) lost no opportunity either in cross-examination of the witnesses or in his speech to the jury of putting forward the theory of murder rather than accident. He even represented Mrs. Jackson's calm and composed demeanour in the witness-box as evidence of the iron nerve which could deliberately put Mr. Allen on the fire. Agitation, hesitation, or confusion in a witness could equally be craved in aid as an indication of guilt. Sir Bernard Spilsbury gave evidence that the death was due to burns; that, when the deceased came in contact with the fire, he was still (whether conscious or unconscious) alive; and that the burning of the head would require exposure to the fire for at least half an hour. He based his opinion on other cases of burning, including the Rouse case. The scalp was burnt away, exposing the skull over the whole of the right side of the head. Over a large area the bone was very thin as a result of the burning; the bone had broken away in the centre of this area. Sir Bernard found it difficult to see how the body could have pitched into the fire of its own motion so as to occupy the position represented in a photograph produced in court. He thought it incredible that Mr. Allen could have been drunk shortly before his death. The length of time during which Mr. Allen's face was in the fire was material in view of the movements of Mrs. Jackson. The jury, after having the two sides of the case fully submitted to them, found a verdict of "accidental death," adding a rider that Mrs. Jackson had nothing to do with it. Some question seems to have been raised as to Mr. Allen's testamentary capacity: the verdict does not preclude the possibility of a probate action in regard to the validity of the codicil.

### What is Iodine Ointment?

It is the statutory duty of local authorities to enforce the Food and Drugs (Adulteration) Act "so as to provide proper securities for the sale of food and drugs in a pure and genuine condition." The annual reports of the Ministry of Health show that vigilance in this respect is necessary. In this connexion recent proceedings undertaken at the instance of the Hammersmith borough council as to the sale of "iodine ointment" are instructive. The formulæ of the British Pharmacopœia, 1914, and the British Pharmaceutical Codex, 1934, require this preparation to contain 4 per cent. iodine and 4 per cent. potassium iodide. On one summons issued last month in respect of a pot labelled "iodine ointment," purchased for 2*d.* in Shepherd's Bush Market, analysis showed no free iodine and no potassium iodide; on another summons, for a pot similarly purchased, analysis showed no free iodine and only 0·4 per cent. combined iodine. These samples consisted mainly of coloured petroleum jelly. Both defendants pleaded guilty and were fined 20*s.* with 21*s.* costs. Early this month a similar summons against F. W. Woolworth and Co., Ltd., was heard at the Kensington police-court. A pot of "iodine ointment," purchased for 3*d.*, was found to consist of iodine 0·06 per cent., potassium iodide nil, combined iodine other than potassium iodide 0·4 per cent., and a base (which was mainly petroleum jelly) 99·54 per cent. Dr. J. B. Howell, medical officer of health for Hammersmith, giving evidence as to the uses of iodine ointment, considered that the amount of free iodine in the Woolworth

sample would be useless as an antiseptic and that the use of such an ointment would confer a sense of false security. The defendant company was fined £15 with 5 guineas costs; it was stated that an appeal would be lodged. The company pleaded a warranty—i.e., that it had bought the article as being the same in nature, substance, and quality as that demanded by the recent purchaser, and with a written warranty to that effect, and that it had no reason to believe it was otherwise, and that the pot was sold in the same state as when originally purchased. Other defences were raised as follows: (*a*) since the current (1932) edition of the British Pharmacopœia no longer includes iodine ointment, there is now no fixed standard; (*b*) as the excise authorities have agreed that the pot of ointment sold by the company is not liable to medicine stamp duty, the pot is not a medicine and is therefore outside the Act; and (*c*) for commercial purposes there is a standard different from that of the British Pharmacopœia and the British Pharmaceutical Codex.

These defences raise points of some interest. As to (*a*) the Food and Drugs (Adulteration) Act lays down no standard of quality and certainly does not incorporate the standard of the British Pharmacopœia. The latter, primarily intended to establish uniform standards for the use of the medical profession in prescribing drugs for their patients, does not pretend to cover a mass of preparations sold for domestic use. As to (*b*) the Act merely says that "the expression 'drug' includes medicine for internal or external use"; it does not say that "drug" means medicine which is liable for stamp duty. There are several articles—borax or carbolic acid, for instance—which have a commercial as well as a medicinal use. In Houghton *v.* Taplin (1897) it was thought that "arsenical soap" containing no arsenic was not a drug. In Fowle *v.* Fowle in the previous year there was a question about beeswax. A sample bought in a grocer's shop was found to be adulterated with 50 per cent. of paraffin. The justices found that prepared beeswax known as "yellow wax" was a substance included in the British Pharmacopœia and used in preparing certain medicines; but they held that the sample was not a drug within the Act, and the Queen's Bench Division agreed with them. It is for the magistrates to decide whether an article is a drug or not. It might, of course, be hard to say that "iodine ointment" was sold for anything but a medicinal purpose. As to (*c*), it is not an uncommon defence to argue that there is a commercial standard which differs from the British Pharmacopœia. In a mercury ointment case in 1901 (Dickins *v.* Randerson) a chemist sold a sample containing 12·5 per cent. of mercury as against the 48·5 per cent. of the British Pharmacopœia. The buyer had not asked for mercury ointment of any particular strength. Several witnesses said that it was the universal practice to supply the preparation in this weaker strength unless the stronger one was either specially demanded or prescribed. The justices held that the Act had been infringed and the Queen's Bench Division decided that an offence had been committed, mercury ointment being a drug in the British Pharmacopœia with a fixed ratio of mercury to fat. Two years later in Boots Cash Chemists *v.* Cowling it was decided that defendants were entitled to show that there was a commercial standard different from that of the Pharmacopœia. This was a case about liniment of soap made with methylated spirit instead of alcohol. The High Court sent the case back to the magistrate (who had rejected such evidence) but offered no opinion itself on the merits. Bell's "Sale of Food and Drugs," where these cases are all mentioned, sums them up by saying that, while the standard of the British Pharmacopœia is not conclusive, very strong evidence is necessary to displace it.

# THE SERVICES

## ROYAL NAVAL MEDICAL SERVICE

Surg. Capts. F. J. D. Twigg to *President* for course, and K. H. Hole to *President* for Medical Depôt, Royal Victoria Yard, Deptford.

Surg. Comdrs. E. Moxon-Browne to *Victory* for R.M. Infirmary, Portsmouth, F. St. B. Wickham to *St. Vincent*, and A. G. Malcolm to *Pembroke* for Sheerness Dockyard.

Surg. Comdr. L. W. Gemmell placed on retd. list.

Surg. Lt.-Comdr. R. C. Foster to *Malabar*.

Surg. Lt.-Comdr. J. G. Maguire to *Ganges* for R.N. Sick Quarters, Shotley.

Surg. Lt. S. K. Foster to *Drake* for R.N.B.

Surg. Lts. W. A. S. Grant to *Medway*, J. G. M. Nisbett to *Sandpiper*, H. L. Belcher to *Tarantula*, and J. W. Rhys to *Penzance*.

### ROYAL NAVAL VOLUNTEER RESERVE

Proby. Surg. Sub.-Lt. D. Shute to be Surg. Sub.-Lt.

D. S. Macphail entered as Proby. Surg. Sub.-Lt. and attached to list 2 of the East Scottish Div.

## ROYAL ARMY MEDICAL CORPS

*Temp. Commissions.*—Maj. J. M. Pinkerton relinquishes his commn. and retains his rank.

Capt. T. L. O'C. Ryan resigns his commn.

Capt. J. C. Gilroy is restd. to the estabt.

### SUPPLEMENTARY RESERVE OF OFFICERS

The undermentioned Lts. to be Capts.: R. M. A. Ormston, P. R. Wheatley, W. F. de C. Veale.

### TERRITORIAL ARMY

Col. P. J. Gaffikin, M.C., M.D., vacates the appt. of A.D.M.S., 44th (Home Counties) Div., on completion of tenure.

Maj. and Bt. Lt.-Col. R. A. Lennie, T.D., M.D., F.R.F.P.S., to be Lt.-Col.

Maj. V. H. Wardle, M.C., T.D., to be Lt.-Col.

H. C. Stewart to be Lt.

## ROYAL AIR FORCE

Wing Comdrs. J. Rothwell to R.A.F. General Hospital, Palestine and Transjordan, for duty as Commanding Officer, H. S. C. Starkey, O.B.E., to Headquarters, R.A.F. Mediterranean, Malta, for duty as Principal Medical Officer, vice Wing-Comdr. D'A. Power, M.C.

Squadron Leader D. G. Boddie to No. 4 Flying Training School, Abu Sueir, Egypt, for duty as Medical Officer.

Flight Lts. H. C. S. Pimblett to Princess Mary's R.A.F. Hospital, Halton, and J. H. Cullinan to R.A.F. Hospital, Cranwell.

Flight Lt. L. I. Hyder is promoted to the rank of Squadron Leader.

## INDIAN MEDICAL SERVICE

Majs. to be Lt.-Cols. R. H. Malone, V. N. Agate, J. P. Canteenwalla, L. S. Modi, H. A. Khin, M. S. Joshi, K. B. Bharucha, H. S. Anand, B. K. Kamakaka.

Lt.-Col. J. Kirkwood retires.

*Embn. M.O., Kiamari.*—Maj. S. O. Dolan, R.A.M.C., has vacated this appointment in India and Maj. A. J. Bado, R.A.M.C., has been appointed.

*Indian Medical Department.*—Maj. (Sen. Asst. Surg.) F. H. Otto retires.

## COLONIAL MEDICAL SERVICE

The following appointments have been made: Dr. A. J. Board becomes Medical Officer, Northern Rhodesia; Dr. J. C. Niven, Malaria Research Officer II., Institute of Medical Research, Federated Malay States; Dr. W. M. Chambers, Deputy Director of Medical and Health Services, Straits Settlements; Dr. R. L. Cheverton, Senior Medical Officer, Falkland Islands; Dr. S. W. T. Lee, Senior Medical Officer, Zanzibar; and Dr. J. I. Moir, Principal Medical Officer, British Honduras.

# PUBLIC HEALTH

## THE PROBLEM OF DIPHTHERIA

### Prevalence

A YEAR ago we drew attention [1] to the sharp rise in diphtheria which took place during the autumn of 1933. The number of notifications was about 20 per cent. in excess of those received during the corresponding period of 1932, and, for each week, between 10 and 20 per cent. above the average (as measured by the median value) of the corresponding weeks of the preceding nine years. We then suggested that the incidence and mortality might be serious during the winter 1933–34, and this has proved to be true. Throughout the late winter and spring of 1934 the notifications remained at a high level but, more important, the usual summer decline of incidence was arrested, so that the excess of cases beyond expectation became higher at the season when prevalence is normally low. When the subsequent course of events is examined (Chart 1), it will be seen that there was again a rapid rise in prevalence from the already high minimum in August, 1934, and in the last two weeks of the year the number of notifications received has, in fact, exceeded expectation by 60 per cent. The actual number of notifications in the 118 great towns of England and Wales during 1934 was 44,367, as compared with 32,585 in 1933. For the whole country they numbered 69,009 as against 47,435 in the previous year, an increase of 45 per cent. The incidence is likely to fall after the end of January, but at what rate cannot be easily predicted. In passing it may be noted that scarlet fever has behaved in a similar way, this concurrence of the two diseases having been constantly observed but never satisfactorily explained.

Recent experience cannot be seen in true perspective without reference to the past behaviour of diphtheria. The Registrar-General gives us each year a statement of the proportion of cases notified in England and Wales to the total estimated population of the country, and these rates are presented in Chart 2 for the years 1911 to 1933. During this period there were two waves of high prevalence, culminating respectively in 1920 and 1930, but the latter declined a little more rapidly than the former. While the interval between them was ten years, a notification-rate almost as high as either of them (1·7 per 1000) has been reached

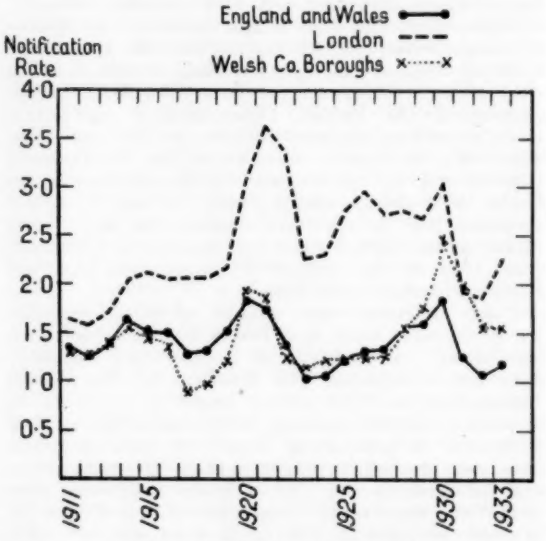


CHART 2. COMPARATIVE PREVALENCE

Notification-rates of diphtheria per 1000 of population during the years 1911 to 1933.
(From the Registrar-General's Statistical Review.)

in 1934—i.e., within the short spell of four years. It is very unlikely that the rise will be continued for a further six years—if it were, public health departments would be faced with a grave problem—but it is at least probable that 1935 will not see any marked abatement. To illustrate what these notification-rates mean, we have charted them also for two areas where they have tended in recent years to be higher than in the whole country—viz., London and the Welsh county boroughs. The consistently high rates in London during the post-war years are attributed by the Registrar-General rather to better observance of the statutory duty of notification than to any pronounced excess of prevalence, and this contention is borne out by the crude fatality-rates based upon deaths and notifications in London which are consistently lower than elsewhere. So far as Wales is concerned, however, this does not appear to be the case, and the principality seems to have been more than usually affected since 1928.

[1] THE LANCET, 1933, ii., 1288.

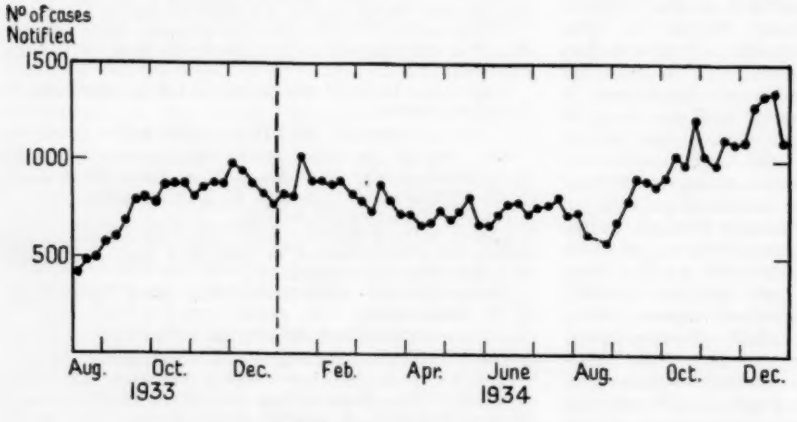


CHART 1. GENERAL PREVALANCE

Notifications of diphtheria in the 118 great towns of England and Wales in each week from August 5th, 1933, to December 29th, 1934.
(From the Registrar-General's Weekly Returns.)

### Mortality

While Chart 2 shows no pronounced tendency on the part of notification-rates to fall during the last 23 years, a similar illustration (Chart 3) of the death-

rates from diphtheria in England and Wales, although it has peaks corresponding with those of Chart 2, shows the mortality during the last ten years to be much lower than the prevalence would have led us to expect. It is difficult to say how much of this apparent fall in fatality is due to better notification

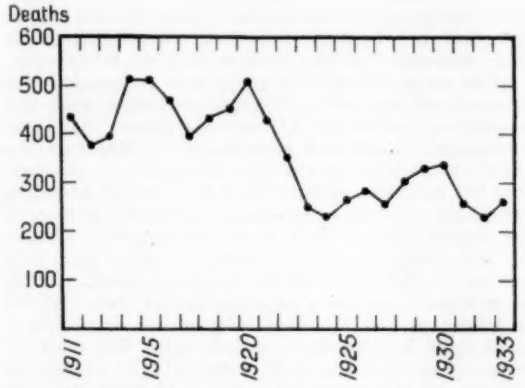


CHART 3. DEATH-RATE IN THE YOUNGER POPULATION
Deaths from diphtheria and croup in England and Wales per million under 15 years of age from 1911 to 1933.

and the use of bacteriological aids to diagnosis, how much to better treatment or how much to a real decline in virulence. The present epidemic may afford evidence which will help to a conclusion. At present we can only record the facts as they appear in statistical returns.

A rough-and-ready measure of the fatality of the disease from year to year may be found in the number of deaths per 1000 notifications in England and Wales (Chart 4). Here the impression gained from examination of the notification- and death-rates is confirmed. The rate during the war years appears inflated owing to defective notification as a result of

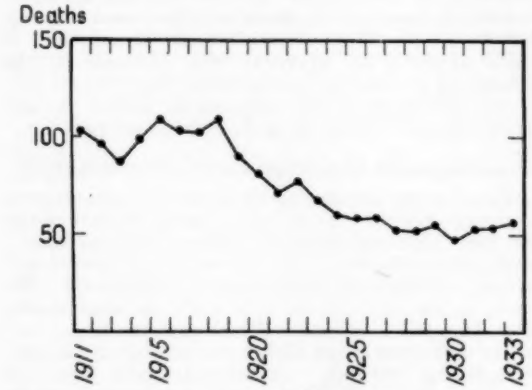


CHART 4. CASE MORTALITY
Deaths from diphtheria in England and Wales per thousand notified cases from 1911 to 1931.

the absence of a large proportion of practitioners on service. If however the decline were entirely due to improved notification, it should be continuous or at least the rate should not increase, since any falling off in this respect is now unlikely to occur. A slight upward tendency since 1930 may therefore be genuine evidence of an increase of virulence which is reported from some parts of the country. The point is further illustrated by the deaths-to-notifications rates in the 118 great towns during 1932, 1933, and 1934:—

| | 1932. | 1933. | 1934. |
|---|---|---|---|
| Cases notified .. .. | 29,976 | .. 32,585 | .. 44,367 |
| Deaths registered .. .. | 1,412 | .. 1,687 | .. 2,334 |
| Deaths per 1000 cases .. | 47·1 | .. 51·7 | .. 52·6 |

The proportion is definitely, if not strikingly, increasing. It is possible therefore that diphtheria is taking a rather more serious form. Even if any increase of virulence were only slight, its association with a continued rise in prevalence would swell the death-rate from the disease.

The actual number of deaths in England and Wales during 1934 is not yet available, but if they have increased in the same proportion as in the great towns they will exceed anything recorded during the last ten years, and this in spite of a steady fall in the number of children at the most susceptible ages.

### The Seed and the Soil

In certain parts of Great Britain and Ireland there has been, as remarked above, an increase in the severity as well as in the amount of diphtheria. Anderson, McLeod, and their colleagues [1] were the first to show (1931) that the exacerbation of diphtheria morbidity and fatality at Leeds was associated with an increased prevalence of special types of diphtheria bacilli—and observation since confirmed in many other localities. It now becomes justifiable to explain variations in the clinical picture, complications, and epidemiological phenomena by observed changes in the types of infecting organisms; one need no longer assume that these variations are caused wholly by unobserved changes in the susceptibility or environment of the human community. The demonstration that severe and epidemic diphtheria tends to be associated with one type of diphtheria bacillus, mild and endemic diphtheria with another kind, is a notable step forward in the epidemiology of the disease. This advance is quite independent of any claim that the "epidemic" virulent variants (so-called *gravis*) and the "endemic" milder (so-called *mitis*) types of diphtheria bacilli are constant in their cultured character or other attributes, when and wherever they are encountered.

Why, at certain intervals and places, the more infective and invasive strains of diphtheria bacilli should appear, or originate from milder endemic strains, is not known. It is however worth recalling that 40 years ago Sir Arthur Newsholme correlated [2] diphtheria epidemics in England, and many other countries, with deficient rainfall. Nevertheless, most authorities did not think that rainfall was a factor of consequence in determining fluctuations in diphtheria rates in comparison with variations in population density and environmental hygiene. No doubt these latter factors would have a greater effect than the weather on the periodicity of diphtheria, provided that they themselves varied. But during the last 20 years in England, environmental and hygienic conditions have, on the whole, improved or remained unchanged. Again Schick-test surveys made during the last decade have given no evidence of any significant decline in the mean susceptibility of the population to diphtheria. It is noteworthy that the very dry summer of 1921 was followed by many local outbreaks of diphtheria, and the present epidemics have materialised during the recent long

[1] Anderson, J. S., Happold, F. C., McLeod, J. W., and Thomson, J. G.: Jour. Path. and Bact., 1931, xxxiv., 667.
[2] Epidemic Diphtheria, London, 1898.

period of deficient rainfall. There may well be something in Newsholme's theory; dry weather may in some indirect way favour the dissemination of the more invasive strains of diphtheria bacilli. If this be so, the present predominance of the virulent "epidemic" types of *C. diphtheriæ* may be expected to subside gradually with the re-establishment of normal rainfall.

### Cases and Carriers

Far more diphtheria infections are caught from carriers than from cases of the disease, because the former so greatly outnumber the latter. Moreover although under identical conditions the case may be a more dangerous source of infection than the carrier, yet most cases are rendered harmless by being isolated in hospital, or at least immobilised in bed, while the vast majority of carriers remain undiscovered and wander freely among their fellows.

Carriers are found to be infected with exactly the same types of bacilli that are found in the cases which are seen at the same time and place. Whether certain kinds of diphtheria bacilli are more prone to produce carriers rather than cases is not known with certainty; but it is possible at one time to have a great prevalence of carriers accompanied by few diphtheria cases, and at another time to have a sharp outbreak of diphtheria with a relatively low carrier-rate—although at both times the percentage of the population having positive Schick reactions is about the same. Certainly some of the "epidemic" strains of *C. diphtheriæ* which are now causing anxiety can produce just as high carrier-rates as are caused by any "endemic" strain which has been investigated.

The carrier-rate depends on a host of known and unknown factors, but other things being equal the rate should be directly proportional to the percentage of the population which is Schick-immune. In practice it can be assumed that all carriers of virulent diphtheria bacilli have negative Schick reactions. On the other hand those in whom the Schick reaction remains positive are susceptible to diphtheria and cannot harbour virulent diphtheria bacilli for any length of time without exhibiting symptoms of the disease. The exceptions to this working rule are too few to invalidate the argument which follows. Further, a Schick-susceptible when attacked by virulent diphtheria bacilli often becomes Schick-immune so rapidly as to escape without noticeable symptoms. This phenomenon, known as latent immunisation, must occur more frequently than attacks of clinical diphtheria, because in urban areas there are only about one in six to one in ten persons who having acquired negative Schick tests have also had clinical diphtheria. There is yet another possibility. When attacked by a virulent diphtheria bacillus the Schick-susceptible may remain Schick-susceptible, but the virulent bacillus becomes avirulent.

It is now easy to see that the greater the proportion of Schick-immunes in a community the greater will be the number of potential diphtheria carriers in that community. It is a peculiar fact that, while artificial active immunisation is an almost absolute protection against clinically recognisable diphtheria, it has no effect whatever in preventing subsequent carrier infection; at the same time and place the virulent carrier-rate is just as high among the artificially immunised as among those with natural negative Schick tests. When a number of children in a school or community are made Schick-immune by inoculation with a diphtheria prophylactic, the density of virulent diphtheria carriers may be correspondingly increased. Such an increase in the carrier-rate has been shown to have followed the artificial immunisation of at least one institution.

### The Individual and the Herd

Should any increase in the density of diphtheria carriers follow on the protection of a part of the community, it will of necessity increase the risk of infection to those who remain Schick-susceptible. This accounts for the well-established observation that an antidiphtheria campaign is in general followed by no significant fall in the diphtheria rates until over a certain percentage of the population has been immunised. American experience is definite on this point. Three years ago E. S. Godfrey showed [3] that the incidence of diphtheria in all of ten American towns did not fall, even after 50 per cent. or more of the school-children had been immunised; directly 30 per cent. of the pre-school children had been protected, diphtheria practically disappeared. Every effort should therefore be made to inoculate children as young as possible, especially as the disease is so much more fatal at the pre-school age. For the same reason it is advisable to immunise all the susceptible children of the same household. If some are protected and others not, the former, should they subsequently become carriers, are liable to infect the latter under the intimate conditions of home life.

The attitudes of the medical officer of health and general practitioner toward antidiphtheria inoculation should be somewhat different. The health authority wishes to reduce the number of diphtheria cases in his whole district. He must therefore prepare a scheme whereby he will ensure that enough children under 5 are protected to achieve this end. Otherwise if he conducts a half-hearted compaign, especially if it is limited to the school-children, he may fail to produce any favourable effect on the diphtheria rates, or conceivably increase them. The general practitioner need not be swayed by such considerations. Every individual has the right to have his children protected on request, even if the risk of infection to those whose parents are too ignorant, or too indifferent, to do likewise is increased thereby. Moreover, provided antidiphtheria inoculation is made available for everyone who demands it, the protection of sensible human stocks from the ravages of *C. diphtheriæ* at the expense of foolish human strains may commend itself on eugenic grounds.

### Inoculation is not Necessarily Immunisation

The necessity of pressing the artificial immunisation of young children becomes more urgent in view of the fact that the illness, caused by some of the "epidemic" strains of the diphtheria bacillus which are in evidence to-day, is relatively irresponsive to diphtheria antitoxin, unless it is given very early in large doses. If a child has been made Schick-immune it is practically safe from *severe* diphtheria, whatever the type of infecting bacillus. Admittedly mild cases of diphtheria do occasionally develop in subjects whose Schick test is negative. In such cases the causative organisms nearly always belong to the so-called *gravis* or *intermediate* varieties of *C. diphtheriæ*. Fatal or severe cases are practically unknown in those whose Schick reaction is known to have become negative after antidiphtheria inoculation. It is, however, quite improper to use the word "inoculated" as a synonym for "immunised" in antidiphtheria work. Some 5 to 10 per cent. of children, according to circumstances, are not made Schick-

[3] Amer. Jour. Pub. Health, 1932, xxii., 237.

immune by a single course of antidiphtheria inoculation. It is just those few children who, because of their inability to respond to the artificially introduced products of the diphtheria bacillus (toxoid, &c.), are the most likely to have a poor response to infection with the living diphtheria bacillus, and who are therefore most likely to contract a severe form of diphtheria. This is the great argument for using the Schick test after each course of inoculation, in order to find out if immunity has resulted, and, if it has not, to go on giving inoculations until the reaction becomes negative. Otherwise repeated reports of severe cases of diphtheria among children, who have been inoculated but never immunised, may cause antidiphtheria inoculation to fall into disrepute.

In a proportion of successfully immunised children the Schick test may become positive again, but this is not of much consequence. Provided a child has once had a negative Schick reaction he has been sensitised against diphtheria toxin; should he subsequently become infected with toxigenic diphtheria bacilli, even though his Schick reaction has relapsed to positive, he responds so rapidly and effectively that he generally escapes symptoms altogether, or only gets a trivial illness. This is not true of inoculated children in whom Schick immunity has never been successfully stimulated.

For the sake of brevity and lucidity many of the questions touched on above have been dealt with dogmatically. For scientific exactitude some of the statements would require qualification. The evidence on which they are based is critically discussed in a recent report[4] by S. F. Dudley, P. H. May, and J. A. O'Flynn to the Medical Research Council.

## INFECTIOUS DISEASE

### IN ENGLAND AND WALES DURING THE WEEK ENDED JAN. 5TH, 1935

*Notifications.*—The following cases of infectious disease were notified during the week: Small-pox, 0; scarlet fever, 2861; diphtheria, 1907; enteric fever, 17; acute pneumonia (primary or influenzal), 1029; puerperal fever, 43; puerperal pyrexia, 109; cerebro-spinal fever, 25; acute poliomyelitis, 8; acute polio-encephalitis, 2; encephalitis lethargica, 5; continued fever, 1 (Tottenham); dysentery, 12; ophthalmia neonatorum, 81. No case of cholera, plague, or typhus fever was notified during the week.

The number of cases in the Infectious Hospitals of the London County Council on Jan. 14th–15th was as follows: Small-pox, 0 under treatment, 0 under observation; scarlet fever, 1413; diphtheria, 2244; measles, 171; whooping-cough, 280; puerperal fever, 19 mothers (plus 7 babies); encephalitis lethargica, 268; poliomyelitis, 8; "other diseases," 290. At St. Margaret's Hospital there were 18 babies (plus 11 mothers) with ophthalmia neonatorum.

*Deaths.*—In 121 great towns, including London, there was no death from small-pox, 3 (0) from enteric fever, 3 (0) from measles, 5 (0) from scarlet fever, 8 (3) from whooping-cough, 65 (10) from diphtheria, 54 (13) from diarrhœa and enteritis under 2 years, and 54 (9) from influenza. The figures in parentheses are those for London itself.

Manchester, Leicester, and Worcester each reported a fatal case of enteric fever. There were 5 deaths from diphtheria at Liverpool, 4 each at Huddersfield and Leeds, 3 at Barking, 2 each at East Ham, Southampton, Bradford, Burnley, Hull, Middlesbrough, Newcastle-on-Tyne, Oldham, Birmingham, and Merthyr Tydfil.

The number of stillbirths notified during the week was 246 (corresponding to a rate of 35 per 1000 total births), including 40 in London.

[4] Spec. Report Series No. 195, H.M. Stationery Office, 1934.

## UNITED STATES OF AMERICA

(FROM AN OCCASIONAL CORRESPONDENT)

### THE SHOCKING WORD SYPHILIS

THE National Advisory Council on Radio in Education has organised for the current radio season a course of lectures on "Doctors, Dollars, and Disease" dealing for the most part with problems of medical economics. An extra lecture in this course was delivered over the long-distance telephone by Sir Arthur Newsholme in London. The fifth lecture in this series was to be on the subject "Public Health Needs," by Dr. Thomas Parran, Jnr., health commissioner of New York State. Dr. Parran had prepared a manuscript in which the possibility of saving life from various diseases was reviewed, and amongst the causes of preventable disease he mentioned syphilis, devoting a short paragraph to the hopeful fact that syphilis can be prevented. At the last moment the Columbia broadcasting system insisted that syphilis must not be mentioned. Dr. Parran refused to cut out the paragraph and the address was not given. The Columbia system issued an explanation in the course of which they point out that "broadcasting reaches persons of widely varying age levels and reaches them in family and social groups." Dr. Parran retorts: "A hopeful view of relief from this dangerous malady might be more welcome to the half million persons in the United States who acquire this disease each year than the veiled obscenity permitted by Columbia in the vaudeville acts of certain of their commercial programmes."

The position taken by Columbia, while typical enough, is not adopted by all American broadcasting stations. Your correspondent has given more than one address over the air in which the word syphilis has been used freely and without objection. The newspapers also are becoming more liberal than in the past and syphilis may sometimes be found now even in the headlines.

### HEALTH OF THE NEGRO

Dr. Louis I. Dublin has recently brought up to date and republished his study on the health of the negro (Metropolitan Insurance Co. Press, New York). The results of displacing the African negro to an entirely foreign geographical and social environment are generally recognised to have had some serious physical consequences. Dr. Dublin shows that in 1930 the coloured death-rate in the United States was 82 per cent. higher than the white; in the cities 95 per cent. higher. The most pronounced difference between white and coloured death-rates is found in the age-group 15–25 years, at which ages the death-rates for coloured males and for coloured females are respectively two and a half and three times those of the whites. In 1933 organic heart disease was the leading cause of death among coloured policy-holders of the company. Second came tuberculosis with a rate of 175·3, more than three times as high as the white death-rate from this cause. Syphilis is only prevalent among negroes and is much more important as a cause of death among them than amongst the white population. Against this unfavourable showing must be placed the remarkable decline in the mortality of the American negro that has taken place in the last two decades. The future holds out a bright prospect for him, so Dr. Dublin believes. The high mortality which he has suffered from such causes as tuberculosis, typhoid fever,

pellagra, malaria, and puerperal conditions has been due, Dr. Dublin argues, to an insanitary environment rather than to any lack of native resistance. The prospects for an improved environment are good. True there are some differences in racial immunity; but the negro has higher resistance against some illnesses, e.g., neurasthenia, diabetes, even if he has a lower resistance to others. His black skin appears to aid him in resisting erysipelas, snake-bites, and in recovering from wounds.

## IRELAND

(FROM OUR OWN CORRESPONDENT)

### THE POPULATION OF THE FREE STATE

THE first attempt at an estimate of the population of Ireland was made in 1672 by Sir William Petty, who also gave figures of those employed in the major occupations; his estimate of the population was 1,100,000. Between Petty's estimate and the first census—taken in 1813—14 estimates were made showing a gradual increase until the figure almost reached 6,000,000. None of these had much claim to accuracy and the first enumeration of importance was that of 1821 which showed a further increase. Thereafter a census was taken in the first year of each decade until 1911. In 1921 the taking was suspended owing to the disturbed state of the country, and in 1926 the first census of the Irish Free State was carried out. The final volume, containing the General Report, was issued last week, and under the editorship of Mr. Stanley Lyon worthily completes the task undertaken by his predecessor, the late Mr. John Hooper.

The population of the Irish Free State on the night of April 18th, 1926, was 2,971,992, being less than the population of the same area in 1911 by 168,000, or 5·3 per cent. It is pointed out that during these years certain abnormal causes of decline were at work: (1) the withdrawal of the British Army of 25,242 with some 34,000 dependants; (2) the number of Irish soldiers killed in the Great War—about 27,405; (3) the number of officers and men who joined the British Army during the war and remained in other countries; and (4) the disbandment of the Royal Irish Constabulary, many of whom left the country. Despite the general decline in population the urban population was steadily increasing. Since 1841 the population has decreased by more than half, and except in Dublin city and county the decline has been more or less uniform all over the country. The Irish Free State has a smaller proportion of females than any other of the 22 European countries, the ratio being 972 females to 1000 males. On the other hand, the proportion is greater than in the United States, Canada, South Africa, New Zealand, or Australia, where the influx of settlers keeps the female population low. During the period 1911–26 births outnumbered deaths by 237,333, so that some 405,000 persons must have emigrated, the number of immigrants being negligible. Of the persons engaged in various industries 53 per cent. were engaged in agriculture, which occupied in all 648,575 persons, or nearly a quarter of the population. It is noted that the proportion of persons over the age of 65 in the Irish Free State is the highest in the world, being exactly double that in the United States. The report contains much information—such as that relating to housing and overcrowding—which is invaluable not only to the statistician but to the social reformer and the doctor.

## PARIS

(FROM OUR OWN CORRESPONDENT)

### CHANGES IN FINGER-PRINTS

A RECENT communication to the French Academy of Medicine must have had a peculiar interest for those whose finger-prints are in the possession of the police and who, however unwilling they may be to turn over a new leaf, might like to turn over a new finger-tip when next examined. This communication was made by Prof. Leonidio Ribeiro, of Rio de Janeiro, who has taken the finger-prints of 200 lepers in all the forms and stages of the disease, and has observed more or less advanced changes in the pattern of the finger-print in 80 per cent. of them. These changes were observed even when there was no macroscopic lesion of the hand or fingers. A microscopic examination, however, made after removal of sections of skin during life, showed active local changes and the bacillus of leprosy. The changes in the pattern of the finger-prints were not permanent in the cases reacting to treatment with chaulmoogra oil. A common change was the appearance of white lines cutting transversely the tracings of the finger-tip; and it was suggested that the demonstration of these lines may facilitate the early diagnosis of leprosy—a possibility of great interest. Prof. Ribeiro has found that sclerodermia with sclerodactylitis also alters the pattern of the finger-print, but the changes in the markings are quite different from those observed in leprosy.

### THE MEDICAL FOREIGNER IN FRANCE

The tightening up of the regulations governing the study and practice of medicine by aliens in France seems to be justified by recently published figures. By 1931, 9·9 per cent. of the medical practitioners in Paris were aliens. In the Seine area in that year, 28·2 per cent. of the persons qualifying to practise medicine were aliens. Between 1909 and 1930, the number of French medical students has increased by only 50 per cent., whereas the number of alien students has increased by 300 per cent. Between 1920 and 1930, there has actually been a diminution in the number of French students in Paris, whereas in the same period the number of aliens has risen from 429 to 1511. A similar state of affairs exists in the provinces. In Tours, for example, 58 per cent. of the students are aliens. Why this invasion? The material facilities for the study of the preliminary subjects in medicine at any rate, are inadequate, according to current British standards. But the general reputation of the Paris school of medicine stands high, and great traditions and great personalities such as Pasteur and Calmette, dead as well as living, exert an undeniable attraction. But what is probably the most important factor of all affecting students migrating from other European countries is *res angusta domi*.

### A BOGUS DIAGNOSTIC REPORT

The diagnostic dossier supplied to a woman patient by an unqualified practitioner has come into the hands of a distinguished neuropsychiatrist who has expressed his appreciation by publishing it in full. The following samples are only a fraction of the whole, but they prove that Madame A. got her money's worth, whatever may have been the fee she paid. An introductory note explains that in the absence of more explicit information, the figure 1 is equivalent to normal. This poor lady's velocity of the internal secretions was only 0·68, whereas her thermic loss

was 2·40. Her cellular vitamin energy was 1·18, and her "masse liquide" was 1·52. The volume of her blood was 6·09 litres, and the velocity of her blood was 0·86, whereas the velocity of her lymph was 1·58. Her vital tension was 5·15 volts, and the length of her vital wave was 597 angstroms. Her state of congestion was 1·22, and her mental agitation was 1·35. Her "potentiel cérébral" was 1·26—surely an exaggeration out of Gallic courtesy to the good lady, whose nuclear divisibility was so far above normal that it reached 4·70. This was presumably a record. Her nervous activity was so great that it could not be expressed in figures, and the diagnostician could give only a vague estimate of it in a laconic "très forte." His less gifted and enterprising colleagues in France are inclined to consider his handling of his patient also as "très forte."

### VITAL STATISTICS OF PARIS

The Prefecture of the Seine has recently published a volume, "Annuaire Statistique de la Ville de Paris" which, though it covers a whole century and deals also with the vital statistics of other localities, is mainly concerned with Paris and the year 1929. Dr. J. Godard (Revue d'Hygiène, December, 1934, p. 725), has extracted some significant facts from this volume with great journalistic skill. These facts are in some respects so ominous that they hardly need the pen of a ready writer to give them prominence. Table XVIII. gives the principal causes of death between the ages of 15 and 24 in Paris in 1929. The most serious cause of death in the young adult is tuberculosis, which is responsible for every other death (49·9 per cent.) at this age. Motors, murders, suicides, and other causes of sudden or violent deaths are responsible for one out of ten (9·8 per cent.) of the deaths of young Parisian adults. Comparable figures for violent deaths from other cities are not given but as far as tuberculosis is concerned the figure of 49·9 per cent. for Paris corresponds to only 18 per cent. (males only) for New York. The actual death-rate in young adults from tuberculosis is even worse than it appears on paper, for notification of tuberculosis as a cause of death is often evaded on account of the stigma attaching to it. Parisians have become much less prolific during the last century, but this movement came apparently to a standstill about 1910. In comparison with other cities, the birth-rate of Paris still holds what Dr. Godard calls an honourable position; it is its death-rate, notably its infant mortality, which is discreditable when comparisons are made with most other cities. Dr. Godard is a constructive Jeremiah, and all who read his lines and between them will find hope for better things. The problem is largely one of health education, social welfare, and a raising of the general standard of living.

### THE DEATH OF PROF. GRANDCLAUDE

A promising cancer research worker has been lost in Prof. Grandclaude, who died recently at the age of 43 from fatal septicæmia following a scratch of a finger in his laboratory. At the time of his death he was assistant director of the anti-cancer centre of Lille. He was formerly attached to the military hospital of Val-de-Grâce in the capacity of director of the bacteriological laboratory, and had also worked later with Prof. Roussy at the Cancer Institute of Villejuif, near Paris.

# CORRESPONDENCE

## MORTALITY FROM PERNICIOUS ANÆMIA

*To the Editor of* THE LANCET

SIR,—While the statistics given by Dr. Hill are not in dispute, their interpretation and the data on which they are based may be open to question. It would be most unfortunate if the practising members of the profession were led to believe that the modern treatment of pernicious anæmia does not constitute one of the greatest advances that has ever been made in medicine.

Prior to the advent of liver treatment in 1926 practically every case of pernicious anæmia died, the average duration of life being about two and a half years after the diagnosis had been established. The mortality-rate for pernicious anæmia has been reduced from approximately 100 per cent. to a low figure, and, in consequence, steadily increasing numbers of cases of pernicious anæmia in the remission stage are accumulating in every country. As pernicious anæmia is essentially a disease of the middle-aged and elderly, such persons are liable, like the rest of the population, to die of intercurrent infection, cardiovascular disease, and so forth. We believe that the source of information on which Dr. Hill has to rely for his statistics—namely, the death certificate—may give misleading information, as we suspect that the name "pernicious anæmia" frequently appears in the certificate as a cause of death when a person who is known to have had pernicious anæmia dies from any cause, even in the absence of anæmia or cord lesions. If this is so, it is hardly to be expected that the fall in the figure for deaths per million from pernicious anæmia which occurred in 1928 as a result of the institution of liver therapy could be maintained. It is necessary to distinguish clearly between mortality figures which refer to the number of persons dying from pernicious anæmia per million deaths, and the mortality figure for pernicious anæmia itself. Dr. Hill suggests that his figures indicate the possibility that liver treatment "may prolong life but not prevent death eventually." We know of nothing which would accomplish this.

While we believe that the criticisms stated above largely explain the Registrar-General's figures of an increased death-rate per million from pernicious anæmia during the last few years, we would stress the fact, recognised by all who have made a study of the disease, that the full benefit of liver therapy is not being obtained. Prognosis is determined by the efficacy with which the blood is continually maintained at a normal level, and for this purpose repeated blood counts must be done, frequently at first, to establish the maintenance treatment necessary, and at least three to four times a year thereafter to ensure that a satisfactory standard is sustained. The value of this after-care was clearly emphasised by Dyke and Harvey (THE LANCET, 1933, ii., 59), who found that of 19 patients attending the Blood Clinic, Royal Hospital, Wolverhampton, regularly, all were alive and well; while 15 out of 33 who failed to report regularly for examination were dead. Our own figures also indicate clearly the value of frequently checking the blood level and adjusting treatment accordingly. Since 1930–31, 75 patients with pernicious anæmia have been admitted to our wards or have attended the blood clinic. Of these 6 are dead. All the fatal cases were admitted at the beginning of 1931; 3 were in the aplastic stage of pernicious anæmia, due to imperfect or absent previous treat-

ment, and failed to respond to all forms of therapy; 3 responded adequately to treatment; of these, 1 refused to continue with treatment, despite all exhortations, and died of sepsis of the urogenital tract; the other 2, who left this district and could not report for follow-up treatment, died, 1, according to her doctor, of kidney disease about a year later, and the other from causes unknown. The remaining 69 cases all keep in good general health, despite the fact that at least 12 were admitted with advanced subacute combined degeneration of the cord. There can be no doubt that without liver treatment at least half of these patients would be already dead. As they grow older deaths will occur among them, as in the rest of the general population, and if their physicians insert "pernicious anæmia" in the death certificate it will be possible to show statistically that the death-rate per million from pernicious anæmia is steadily increasing.

We are, Sir, yours faithfully,

STANLEY DAVIDSON,
HAROLD W. FULLERTON.

Aberdeen, Jan. 9th.

*To the Editor of* THE LANCET

SIR,—Dr. A. Bradford Hill in your issue of Jan. 5th provides statistical evidence showing that after a sharp fall in the years immediately following upon the introduction of liver treatment the mortality from pernicious anæmia up to 1933 had again risen. The 1933 level is lower than that of 1932, and it is possible that this latter year represents the peak of the mortality; none the less the fact that there should have been a rise at all is disquieting. It is particularly so because the experience of everyone having extensive acquaintance with the treatment of pernicious anæmia indicates that it is entirely avoidable; uncomplicated pernicious anæmia at the present day should have no mortality at all. There is no gainsaying the words of Sir George Newman, quoted by Dr. Bradford Hill, that in pernicious anæmia "a fatal termination may now be indefinitely postponed in the majority of cases."

Why then the increase in the mortality from this disease? The answer appears to be that it is one thing to make available a specific remedy and quite another to secure its intelligent use. The question of the diagnosis and treatment of pernicious and other anæmias was discussed at the summer meeting of the Association of Clinical Pathologists held at Manchester in 1933. The discussion, which was fully reported in your columns at the time (THE LANCET, 1933, i., 78), made it clear that failure of liver treatment depends (1) upon the use of liver in the treatment of anæmias other than of the "pernicious" type, and (2) upon inadequate dosage. Dosage may be inadequate either by reason of the use of too small amount of a potent preparation or by reason of the use of an impotent preparation in what would be adequate dosage for a potent one. It was further made evident that the diagnosis of pernicious anæmia cannot be established without the assistance of laboratory methods, and that without the use of such measures it is impossible to gauge with accuracy the response to treatment and to establish the dosage of the anti-anæmic principle required by any given patient at any given time.

The association passed unanimously the following resolution of which copies were sent to the Ministry of Health, the Medical Research Council, the Association of Secretaries of National Health Insurance Committees, the British Medical Association, and other bodies which it might be supposed would be interested:

"That this association is of the opinion that the failure to provide laboratory facilities for patients under the National Health Insurance Acts suffering or supposed to suffer from anæmia is responsible for much wastage both of efficiency and life and considers that such laboratory service should be made available in recognised centres both for initial differential diagnosis and for the periodical examinations necessary to maintain a sound state of health."

Pending the organisation of some general service for the diagnosis of and the control of the treatment of anæmia this association has done its best to encourage its members, where local circumstances permit, to establish anæmia clinics in connexion with their own laboratories. A number of such clinics are now associated with the pathological departments of various voluntary hospitals throughout the country; this is possibly a factor in the fall in the mortality-rate from pernicious anæmia in 1933 as compared with 1932, as shown in Fig. 1 of Dr. Hill's paper.—I am, Sir, yours faithfully,

S. C. DYKE,
Hon. Secretary, the Association of Clinical Pathologists.

Wolverhampton, Jan. 13th.

## IMMUNISATION AGAINST YELLOW FEVER

### VACCINATION AND SERO-VACCINATION

*To the Editor of* THE LANCET

SIR,—In a paper in your issue of Nov. 3rd, 1934, Dr. G. M. Findlay expresses objections to the method of vaccination which is used against yellow fever in French West Africa. This method, as is known, makes use of the living virus alone—that is, without the addition of protective serum. Findlay bases his opinion on the results of ten experiments on monkeys. He brings forward no direct proof concerning man.

The French colonial physicians, who are used to these vaccinations, continue, however, to use this method with confidence; they believe that there is no reason to restrict its application. They have generalised it in Senegal, Ivory Coast, Niger, Sudan, Guinea, Dahomey. Out of the thousands of human vaccinations which have been effected in these colonies there has resulted no single serious accident for the vaccinated persons or the community. Therefore Findlay's objections have no weight as regards human vaccination. His experiments, besides, were conceived and undertaken before he knew the results of the application of the method in French West Africa. He does not speak of this priority which is easily established: ten days only after the publication of our note, at the Académie des Sciences, concerning vaccination in West Africa,[1] there appeared the work of our English colleague. Seventy-five days at least were necessary to terminate the experiments of which he speaks.[2]

On several points Findlay comments favourably on our method. For example, concerning the preparation of our vaccine he states that he obtained, without difficulty, the regular ageing of the virus at 20°. He verified that out of ten monkeys on which he experimented, one having been killed before the end of the experiment, nine acquired immunity. Seven were immunised by the first vaccination alone. Against our method Findlay holds that the monkeys' blood was virulent (for mice) during the first week of the vaccination, and that one of the vaccinated animals contracted encephalitis. He deduces that the multiplication of the virus in the organism is necessary in the establishment of the immunity, by

[1] Mathis, C., Laigret, J., and Durieux, C.: Compt. rend. Acad. des Sci., 1934, excix., 742.

[2] Preparation of the vaccine by our technique: at least 20 days. Observation of the monkeys after the first vaccination: 20 days. Observation of these animals after the second vaccination: 20 days. Proof of their immunity: at least 15 days.

our method, and that the infection thus obtained can easily overcome the "barrier" which separates the blood from the nerve centres, and cause serious disorders in the latter.

The multiplication of the virus in the vaccinated organism is without doubt the essential condition of the immunity. The sterilised amaril virus no longer vaccinates. We use the living mouse virus to bring about an infection, which is generally imperceptible, or which is sometimes limited to a benign fever of a few hours' duration, and which later immunises against the attacks of the natural, or, if one prefers, the normal, amaril virus. This is true not only for our method but also for that of sero-vaccination which Findlay himself currently uses in man. In neither case is there an active immunisation without a previous infection, even though imperceptible, by the living virus. It is probable that this infection is general from the start; it seems that it never meets a "barrier"; at any rate, the nerve centres always participate in it, more or less. The symptomatology of the disorders or, rather, the discomfort felt by a great number of vaccinated persons, clearly indicates this. But the intensity of this infection is so feeble that with our present methods of research we are unable to prove the virulence of the blood.

It is because Findlay inoculated his monkeys with doses which are relatively strong for these little animals that he has been able to infect mice with their blood. Sawyer, with sero-vaccination, has obtained the same result: monkeys which receive little serum and much virus furnish, during a few days, blood which is virulent for mice.[3] One cannot even affirm that the positive inoculation of mice is proof, in such cases, of the virus's multiplication within the vaccinated organism; perhaps one simply finds, in the blood which is taken during the first few days, the excess virulent material which has not been destroyed. At any rate, under the conditions of our work, in man, up to now, the blood of even febrile vaccinated persons has never been virulent for mice. But even if it were virulent, this fact would have no importance per se.

The only fear one could harbour was that the living vaccine, transmitted by mosquitoes from vaccinated to non-vaccinated persons, could communicate yellow fever. But this return to virulence has never occurred under the conditions of human vaccination. In experiments as yet unpublished Mathis, Durieux, and I have fed each day, for 20 days, different lots of mosquitoes on vaccinated persons at Dakar. These mosquitoes were placed on unvaccinated men, and were finally ground up and inoculated into several *Macacus rhesus*. Neither the unvaccinated men nor the monkeys became ill; nor were they immunised. Besides, vaccination has been carried on in Senegal, in regions infested with stegomyia, and in Niger and Ivory Coast, in regions where there is yellow fever, and everywhere we have proof that it is not dangerous for those in contact with the vaccinated.

There remains, for the vaccinated person, a slight but real risk—that of a meningeal reaction. Neither the frequency nor the magnitude of this risk can be judged by the experimental vaccination of macacus. These monkeys are more sensitive than man to yellow fever, which manifests itself in them by a brief and fatal attack; they are also more sensitive to the attenuated mouse virus. They die of encephalitis, in cases where it follows the inoculation of the virus. The first 3000 human vaccinations which were done in Africa, on the contrary, have been followed in only 2 cases by nervous reactions, and in both of these the vaccinated persons recovered without sequelæ. One may infer from these results that the risk of the anti-amaril vaccination in man is limited to a meningo-encephalitic (or meningo-myelitic) reaction which occurs in one case out of about 1500 vaccinations and which, up to now, has ended in complete recovery within a few days. This risk is of no account in comparison with the danger which besets unvaccinated people in countries where yellow fever exists and in others which it may overrun.

Findlay, comparing sero-vaccination and our method, states that the latter is the more practical, since it eliminates the complication and the inconvenience of serum. This judgment may be—and we hope that it will be—the conclusion of a debate which has no longer any significance since the demonstration of the activity and the innocuousness of the method on thousands of people in the colonies. This work has gone out of the laboratories; it now belongs to the practitioners. Those who carry it on with enthusiasm in French West Africa, and those who plan to organise it wherever yellow fever threatens, should be encouraged.

I am, Sir, yours faithfully,

J. LAIGRET,
Chef de Laboratoire, Pasteur Institute, Tunis.

Paris, Jan. 8th.

[3] Sawyer, Kitchen, and Lloyd: Jour. Exp. Med., 1932, lv., 945.

## FRACTURES INVOLVING THE POSTERIOR FOSSA OF THE CRANIAL BASE

*To the Editor of* THE LANCET

SIR,—Mr. L. Bathe Rawling has recently published a monograph on "Injuries of the Head," which was reviewed in THE LANCET on Nov. 17th, 1934, p. 1109. In his book he says that: "There are no external hæmorrhages in fractures of this fossa other than one occasional ecchymosis behind the ear, in relation to the mastoid-occipital suture or over the line of a fracture traversing the cerebellar fossa."

In THE LANCET for July, 1890, were published three lectures which I had delivered at the Royal College of Surgeons of England, as Hunterian lecturer, under the designation "Injuries of the Head." In those lectures special attention was given to fractures of the posterior fossa of the base of the skull. Some of the patients had died after admission so that a full description with post-mortem examination was possible. All of them were hospital patients under my personal observation as surgical registrar (five years) or resident assistant surgeon (three years), and for another period of two years as assistant surgeon to the Royal Free Hospital before the lectures were given. The observations were confirmed by many others, and post-mortem reports were supplied by the pathologist when the injury had proved a fatal one. In one case, where death followed from tuberculosis some time afterwards, diagnosis had been made from the symptoms after admission, of double fracture of the base, and the report from the pathologist confirmed the diagnosis in every respect.

May I refer your readers to the report of this and other cases as recorded in the second of these Hunterian lectures. The time of appearances of ecchymosis was as follows: 6 on third day; 3 on fourth day; 4 on fifth day; 1 on sixth day; 2 on seventh day; 1 on twelfth day. Others uncertain. Cases of fracture in this situation with hæmorrhage over mastoid after admission were observed in 21—recovered, 11; died, 10.

I am, Sir, yours faithfully,

Horsell Common, Woking, Jan. 15th. W. H. BATTLE.

## THE WALTER FLETCHER MEMORIAL

*To the Editor of* THE LANCET

SIR,—In your issue of June 16th, 1934, you printed a letter from Mr. Stanley Baldwin and others, including the undersigned trustees, proposing a tribute to the memory of the late Sir Walter Morley Fletcher, first secretary of the Medical Research Council. Subscriptions were invited to a fund to be used in the first place for a personal memorial at the National Institute for Medical Research at Hampstead, and in the second place towards the cost of building a Walter Fletcher Laboratory at Mill Hill for nutritional investigations. We are now glad to record that the response has been no less than was confidently expected, and that the means for giving effect to the projects are assured.

The total brought by the appeal already exceeds £2000, and it is believed that there are still many who intend to contribute before the fund is closed. It is an appropriate result that a great part of this sum is made up of small subscriptions from a large number of research workers and others, although donations of substantial amount have also been received.

We are, Sir, yours faithfully,

DAWSON OF PENN,
H. H. DALE,
T. R. ELLIOTT,
E. MELLANBY.

Jan. 14th.

## MONOCYTIC LEUKÆMIA

*To the Editor of* THE LANCET

SIR,—In the paper by Drs. Whitby and Christie appearing in your last issue I am credited with having made hæmatological statements, and with holding certain hæmatological beliefs, which I disclaim completely; never having made or held them.

"Naegeli maintained that the monocytes described were unusual forms of myeloblasts, a view which even to this day is supported by Piney." Here the authors mention page 178 of the third edition of my "Recent Advances in Hæmatology" as authority for this statement, but the only relevant remark that occurs on this page is "Naegeli's view that it (monocyte) belongs to the myeloid series of leucocytes seems, on the whole, more satisfactory than the conception of an origin from a third hæmatopoietic system. . . ." The sentence, following the first one quoted above, reads: "It must, however, be borne in mind that both Naegeli and Piney regard the monocyte as a cell derived directly from the myeloblast." But on page 26 of the book the authors do me the honour to quote I say that the term "promonocyte" is preferable to "monoblast," because the latter implies that the monocytes have a separate genealogical history. Surely it is clear that my contention is that the monocyte is not derived directly from the myeloblast, but that I believe that an intermediate cell-form, the pro-monocyte, can be distinguished. So far as I know the only writer who has ever contended that monocytes were altered myeloblasts was Ziegler, but the view never found acceptance.

After this defence of my position, may I attack another statement that appears in the paper by Whitby and Christie? "The appearance of myeloblasts in the terminal phases has been recorded by other observers and does not, in our opinion, justify a diagnosis of myeloblastic leukæmia, but merely suggests that the myeloblast and 'monoblast' have a common precursor cell."

Now, in many cases of chronic myeloid leukæmia in which myelocytes dominate the blood picture for months or years, there may be great myeloblastosis in the terminal acute stage. The number of myeloblasts in the blood may be so great as to make it impossible, except on clinical grounds, to distinguish the condition from a primarily acute myeloblastic leukæmia. It has been, and still is, usual to adduce this fact as evidence in favour of the view that myelocytes are derived from myeloblasts, but Whitby and Christie would presumably contend that it merely suggests that the myeloblast and the myelocyte have a common precursor cell! If, however, they would agree to the commonly accepted interpretation of the fact, their argument in favour of the fundamental distinction between myeloblast and "monoblast" fails to carry conviction. And when they say, "The case, as judged by histological sections, appeared to present a partial myeloid termination . . ." my view that the monocyte is a myeloid cell is strengthened rather than weakened by their observations.

The very fact that a leukæmia which starts with a monocytic blood picture runs a less acute course than does a primarily myeloblastic leukæmia supports my view, because it is a commonplace that the more differentiated the predominant cell-type the less acute the course. This is clearly shown in Whitby and Christie's case; and I have observed it in two cases (unpublished): one of a lady aged 72, and the other a man of 67. The former died six months after the onset of symptoms, and the latter lived for 18 months. Incidentally, in both of these cases there was enlargement of the liver, but not of the spleen.

It is unfortunate that there is so little information concerning the number of thrombocytes in monocytic leukæmia. In the case of the woman mentioned above, these elements were normal in number and structure throughout the illness, whereas in the man there was thrombocytopenia (down to 40,000 per c.mm.) during the last three months of life; and there were many poikilothrombocytes. Both cases were treated with Campolon and calcium gluconate, with only transient improvement.

I am, Sir, yours faithfully,

A. PINEY, M.D., M.R.C.P.

Park-square West, N.W., Jan. 13th.

## MAGNESIUM SULPHATE IN ACUTE INTESTINAL STRANGULATION

*To the Editor of* THE LANCET

SIR,—In his valuable article on Prognosis in Acute Intestinal Strangulation (THE LANCET, Jan. 12th, p. 103) Mr. Claude Frankau states that the only safe drug to give by mouth is magnesium sulphate, as it acts purely by osmosis and helps to sweep away toxic products. From my much more limited experience I would agree about its value, especially when given at the same time as an injection of pituitrin, but not with his explanation. Over 25 years ago Mr. Frank Cook and Mr. E. G. Slesinger, then students at Guy's Hospital, carried out some experiments with me, reported to the Therapeutical Section of the Royal Society of Medicine (see THE LANCET, 1908, ii., 1444), which proved that, whatever may occur in animals, saline aperients in man act only after absorption into the blood stream and not by attracting water into the lumen of the bowel. A watery stool is passed before the salts have reached the cæcum, but not before some has been absorbed and excreted in the urine. The watery stool generally contains none of the salt, some of which is rapidly excreted in the urine

and the remainder in the formed stool passed the following day—a conclusive proof that its mere presence in the bowel does not attract water into the lumen.

I am, Sir, yours faithfully,

Jan. 14th. ARTHUR F. HURST.

## PHYSICAL EDUCATION

*To the Editor of* THE LANCET

SIR,—The commentary in your last issue (p. 127) on Mr. H. E. Naylor's address to the British Association for Physical Training at the Conference of Educational Associations, and the recent lecture by Prof. L. P. Jacks at the conference of young public schoolmasters at Harrow School, coupled with the announcement that the British Medical Association proposes to consider the question of physical education, suggest that the subject of physical fitness in the general population is at last to be given not only earnest thought, but also the practical attention which it warrants from the national and individual points of view. Prof. Jacks again makes an eloquent plea for raising the status of teachers of the subject, and your readers will be reminded that in his Lloyd Roberts lecture delivered before the Royal College of Physicians in 1932 (THE LANCET, 1932, ii., 1145), he spoke very forcibly on the need for compulsory physical education. "I can think of no more effective means," he said, "of countering that terrible process of human damage that is going on in our cities and which, if it goes on unchecked, will defeat all the other efforts we are making, whether political or educational, to put our affairs on a better footing. All other problems seem to me secondary to that of raising the quality of the human material in the masses of the people. If that goes down nothing else will go up, no matter what changes you make in political institutions or in the social system."

The British Association for Physical Training has long been striving for the proper recognition of physical education. The Association instituted its own examinations many years ago, and to become a fully qualified teacher a candidate must possess a sound knowledge of human anatomy, physiology, hygiene, theory of physical education, and school remedial exercises as well as of the teaching and practice of educational gymnastics and games. Last, but not least, the candidate has to pass searching practical tests of his or her ability as a teacher of a class. Within recent years, the University of London has instituted a diploma of physical education, but as far as I am aware there is no single institution in London where a young man can attend the requisite courses of instruction. Ten years ago the British Association for Physical Training put forward a scheme for the establishment of a training centre in London for teachers, but funds were not forthcoming. Perhaps something may now be done.

I am, Sir, yours faithfully,

G. P CROWDEN,
Chairman of Council, British Association for
Jan. 14th. Physical Training.

## BLOOD-STAINED TEARS

*To the Editor of* THE LANCET

SIR,—The annotation under this heading in your issue of Nov. 17th, 1934 (p. 1115) leads me to relate a similar case recently under my care.

A girl, aged 3½ years, child of a Gurkha rifleman, was brought to hospital with the history that for the last three months whenever she cried blood and not tears came from the eyes. The child was examined but no abnormality could be detected in the conjunctiva or lacrymal apparatus; the general health was satisfactory and no marked anæmia was present. An iron mixture was prescribed and the parents instructed to bring the child again to hospital should no improvement occur. Three weeks later she was again brought to hospital and this time, luckily, cried on examination, when there was no question of the parents' story being accurate; actual blood, somewhat diluted by tears, was observed running from the eyes. The child has now been under observation for three months, and at the present time the condition has almost cleared up, the tears now being only tinged a faint pink. In view of the child's age this case can hardly be one of vicarious menstruation.

I am, Sir, yours faithfully,

R. L. HAVILAND MINCHIN.

Indian Military Hospital, Abbottabad, N.W.F.P., Jan. 7th.

## THE ALLEGED NEED FOR MEAT BY THE YOUNG

*To the Editor of* THE LANCET

SIR,—In a pamphlet entitled "The Day's Food: Six Months to Twelve Years," issued by the British Broadcasting Corporation, the statement is made: "There is a mistaken idea that it [meat] is not needed by the young, but this is not so, as, on the contrary, it is *most necessary for growth*." (The italics are my own.) On being challenged to produce the authority for a statement so entirely contrary to what is now a great mass of vegetarian experience, the Corporation replied: "Our arrangements with the General Medical Council preclude the disclosure of the author's name, but we can assure you that he is in fact a first-class authority on diet"; and renewal of my society's representations has been met with a similar refusal either to withdraw or to amend.

May I be allowed the courtesy of your columns in contradicting the statement from the pamphlet which is above quoted; surely in the interests of truth itself—which also are those of the public welfare—it is of importance that it should not go undenied? Evidence from medical and scientific sources, apart from vegetarian experience, would seem to be quite conclusive. For the sake of brevity I mention but three authorities. It was the decision of the International Scientific Food Commission, which met in several European capitals during the Great War, that "no absolute physiological need exists for meat, since the proteins of meat can be replaced by other proteins of animal origin, such as those contained in milk, cheese and eggs, as well as by protein of vegetable origin"; Prof. E. V. McCollum has declared that "we could entirely dispense with meats without suffering any ill-effects whatever"; whilst Sir Robert McCarrison (who, doubtless, in making his statement, had in view also the importance of other food constituents, apart from proteins) says categorically in his small primer entitled "Food," which is written specifically for the instruction of the Indian peoples: "If the food contains enough milk and milk-products then it is not necessary to eat flesh-meat at all."

I am, Sir, yours faithfully,

FRANK WYATT,
Jan. 15th. Secretary, London Vegetarian Society.

WILLESDEN MATERNITY HOSPITAL.—Sir Comyns Berkeley has opened an extension to this hospital. The total number of beds is now 58 and the hospital will be able to receive about 1000 cases a year. Among the 494 treated last year there was no maternal death.

# OBITUARY

## JAMES FERGUSON LEES, C.B.E., M.D. Glasg.

LATE DIRECTOR-GENERAL OF PUBLIC HEALTH, MINISTRY OF INTERIOR, CAIRO

WE regret to announce the death, which occurred on Saturday last, Jan. 12th, at Little Manston, Cornwall, of Dr. Ferguson Lees who was widely known for his important sanitary work in Egypt.

James Ferguson Lees was born in 1872 and educated at the Stanley House School, Bridge of Allan, and the University of Glasgow. He graduated as M.B., C.M. Glasg. in 1893 and acted as house surgeon to the Hartlepool Hospital. He was for a brief time in the service of the City Line and African steamship companies, and also held the appointment of pathologist to Durham County Asylum. During the South African war he served in charge of a hospital ship and at a base hospital and finally with the first battalion of the Connaught Rangers; at the conclusion of hostilities he was awarded the Queen's medal with three clasps.

Lees's long connexion with Egypt commenced with his appointment as P.M.O. at the Nile Reservoir Construction Works at Assouan and the Isna barrage, and in 1908 he joined the Egyptian Government service as port health officer, Port of Alexandria; in 1910 he was chosen as M.O.H. for Cairo city, receiving in 1913 the order of commander of the Imperial Ottoman Order of the Medjidieh in recognition of valuable work. The European war therefore found him with special qualities for valuable work. He served with the Egyptian Expeditionary Force, and was later appointed inspector of the prisoner of war camps in Egypt, and for these and other services and duties discharged in connexion with the war he received numerous decorations, and was appointed commander of the Order of the Nile. After the war he became deputy director-general, public health, and in 1920 director-general, a post which he held for five years during which time he acted as Under-Secretary of State in the Ministry of the Interior. He received the C.B.E. in 1922 and was appointed grand officer of the Order of the Nile in 1923.

Dr. Lees married in 1926 Dorothy Page, daughter of Mr. John Newton, of Bridgeham, who survives him and by whom he had one son and one daughter.

## ANDREW WYLIE, M.D. Glasg.

WE regret to announce the death from a drowning accident of Dr. Andrew Wylie, the well-known laryngologist. The tragedy occurred at Bridge of Allan on Saturday last, Jan. 12th.

Andrew Wylie was born in 1869, the son of Mr. John Wylie, J.P., of Hamilton, and was educated at the universities of Glasgow and London. He graduated as M.B., C.M. Glasg. in 1891, with honours in several directions, and proceeded to the degree of M.D. Glasg. in 1896, and thereafter did post-graduate work in London, Paris, and Vienna. He held resident and other appointments in London, among others that of clinical assistant at the Central London Throat, Nose and Ear Hospital. Here in due course he became registrar, assistant surgeon, and full surgeon, and was the senior officer on the staff at the time of his death. He soon became known to his colleagues as well as to the public as a skilful aurist, while he read practical communications before the old British Laryngological, Rhinological, and Otological Association, of which body he became secretary; it is now merged in the Royal Society of Medicine. He published a treatise on laryngeal growths and another in which he dwelt on the value of hot-air treatment in certain forms of deafness, and continued to make communications to the laryngological and otological sections of the Royal Society of Medicine, becoming president of the former. He was a corresponding member of the Société Française de Laryngologie and was a widely known representative of his specialty in this country and abroad.

## WILLIAM ARTHUR EVELYN, M.A., M.D. Camb.

SENIOR PHYSICIAN, THE YORK COUNTY HOSPITAL

THE death occurred on Sunday, Jan. 6th, at his residence in Clifton, York, of Dr. William Arthur Evelyn, senior physician to the York County Hospital. In addition to his distinction as a medical man he was a well-known antiquary and art collector, while in younger life he was a notable sportsman. He was 73 years of age and had been of later years in very delicate health. The portrait reproduced shows him in middle age.

William Arthur Evelyn was the son of Francis Lyndon Evelyn of Kinsham Court, Radnorshire, and was educated at Charterhouse, whence he went to Caius College, Cambridge. He graduated in arts and proceeded for his clinical training to St. Thomas's Hospital; he took the English double diploma in 1887 and in the same year graduated as M.B. Cambridge. After holding resident appointments, among others that of house physician at Brompton, he was initiated into private practice by acting as assistant in a firm of medical practitioners at Reigate of which Sir Constantine Holman was the senior partner. In 1891 he began his long connexion with the city of York by entering into partnership with the late Mr. William Hamerton Jalland, at whose death he became the head of a large and old-established practice. He was elected physician to the York County Hospital, and soon began to take a prominent part in the conduct of the institution in addition to his clinical duties, eventually becoming chairman of the medical board. He was prominent also in the foundation of the local society for the prevention of tuberculosis and in all work associated with maternity and child welfare, and was active in the interests of the St. Stephen's Orphanage.

DR. EVELYN

He was chairman of the local division of the branch of the B.M.A. But the influence that Evelyn exercised over the city of York and the district is not indicated

by this recital. It was his interpretation of the duties which he undertook which made him a centre both of medical work and of much and varied endeavour for the public welfare. When he undertook anything, either as an individual or through a committee, he was resolute, almost relentless, in performance, and he thus acquired a position of authority which he never set out to attain.

Evelyn was devoted to the city of York, and unsparing in his efforts to preserve its ancient monuments and beauties, while the vandalism of the past was an abiding source of sadness with him. Throughout the more than 40 years during which he lived and practised in York he was an open-handed but discriminating collector of pictures and prints illustrating the history, the ancient appearance, and the architectural relics of the city. The pictures which he brought together formed one of the finest collections in the country, designed to expose the growth, life, and history of a historic centre. Included in it were oil paintings, water colours, wash and pencil drawings, etchings, engravings, lithography, and original copper-plates—in all about 1200 works. Such artists as Copley Fielding, Girtin, Pyne, Rowlandson, and Varley were represented, and the collection became, by the time that Evelyn was reconciled to its dispersal, of high value, many of the works being by painters whose pictures must command big prices in the sale-room. Evelyn, however, was particularly anxious that a home should be found for the collection in the centre of its inspiration, and he offered to dispose of it to the city of York for a sum far from representing his outlay upon it. The city accepted the offer about two years ago, and the Evelyn collection is now housed in the York Art Gallery.

At school, at college, and for some years later Evelyn was a prominent exponent of many games. He was a good cricketer and lawn tennis player, while at football under Association rules he was a brilliant performer; the Old Carthusian football club, one of the few amateur teams that has held the Association football cup, was at the top of its form when Evelyn was captain of the team.

Dr. Evelyn married Constance Margaret, daughter of the late Charles Hardman of Reigate, who survives him, with two sons and three daughters.

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### WALTER SALISBURY, M.D., M.S. Lond., F.R.C.S. Eng.

WE regret to record the death of Mr. Walter Salisbury, surgeon to the Northampton General Hospital, which occurred on Monday, Jan. 7th, after a very short illness from influenzal pneumonia—he was actually at work on the Sunday preceding his death—at the untimely age of 46.

Walter Salisbury was born in Bristol, the son of Mr. F. G. Salisbury, and was educated at Wycliffe College, the University of Bristol, and the University of London, following his later clinical courses at St. Thomas's Hospital. He qualified in 1913 with the English double diploma and graduated in the University of London as M.B., B.S. in 1913. In 1920 he proceeded to the M.D. degree (Gynæcology), and the following year took the degree of M.S. Lond. and in 1923 the diploma of F.R.C.S. Eng. Among his earlier appointments were those of medical resident officer at Queen Charlotte's Hospital and the Bristol General Hospital, the Women's Hospital, Soho-square, and house surgeon to the Royal National Orthopædic Hospital. In 1915, with the rank of captain, he was surgeon-specialist attached to the R.A.M.C. In 1925 he was appointed to the staff of the Northampton General Hospital, while he was also holding the posts of consulting surgeon to the Manfield Orthopædic Hospital, Northampton, and consulting obstetrical surgeon to the Northampton borough and the Northamptonshire and Rutland county councils. He was at one period secretary and treasurer of the Northampton branch of the British Medical Association and wrote in the *British Medical Journal* on the action of cutaneous anæsthetics and malignant disease of the chorion, whilst he also contributed to the Proceedings of the Royal Society of Medicine papers on the obstruction of labour by ovarian cysts and on the diagnosis of diaphragmatic hernia. He took the diploma of M.C.O.G. and was a Fellow of the Association of Surgeons of Great Britain.

The death of Mr. Salisbury inflicts a second loss on the staff of the Northampton General Hospital with which all will sympathise, for only a few days previous to Mr. Salisbury's death the death occurred, as recorded in our columns last week, of Mr. Basil Laver, also surgeon to the hospital, and only 40 years of age.

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### HARRY ALBERT MURPHY, L.R.C.P., L.R.C.S., L.M. Edin.

Dr. Murphy, whose death occurred at Southport on Dec. 30th, was the eldest member of the large family of a Bolton dentist, Mr. Thomas Murphy, who is stated to have been the first qualified dentist in the district. Harry Murphy received his medical education at Owen's College, Manchester, and qualified with the Edinburgh triple diploma in 1882. He held the appointment of house surgeon at the Manchester Royal Infirmary and then joined as surgeon the Ocean Steamship Company in whose service he made several voyages to China. On retirement from that service he practised for a time at Bolton, but some 20 years ago transferred to Preston, where until recently he had lived. While at Preston he coöperated in a piece of work with which his name will be long associated. He was concerned at the incidence of tuberculosis among the weavers, and in conjunction with a local electrical engineer, Mr. J. F. Simpson, invented a contrivance, the Murphy-Simpson shuttle, designed to prevent the dangerous practice of shuttle-kissing. The apparatus was described in these columns (THE LANCET, Jan. 7th, 1911, p. 129).

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FAREWELL DINNER TO PROF. GREY TURNER.—On Jan. 11th Prof. G. Grey Turner was entertained at a civic dinner in the Mansion House at Newcastle-on-Tyne. In proposing his health the Lord Mayor (Mr. Councillor Stanley Dalgliesh) said they were met to honour a man whose reputation extended far beyond Newcastle and who was loved in his native city not only for his efforts to improve the conditions of human life but for his modesty and simplicity. Prof. Grey Turner, in replying, admitted that he was born at North Shields and cherished a great admiration for the work done by city fathers. He regretted that the insistent duties of medical men left them little time for public work, but while making no excuse for not having participated in civil affairs he could advance a claim made by a fellow Northumbrian. This man, he said, had a large family and he had never paid his doctor one penny. On one occasion when the doctor hinted that his financial obligations were neglected the man replied: "Well, I can say, Doctor, you have always had my loyal and devoted support." Prof. Grey Turner said that the London post was not of his seeking; he had accepted because he felt it was due to the school to which he belonged and that he was forging another link between north and south.

# MEDICAL NEWS

## Royal College of Surgeons of England

A quarterly meeting of the council was held on Jan. 10th, with Sir Holburt Waring, the president, in the chair. Mr. Ralph St. Leger Brockman, of the University of Sheffield, was admitted as a member of the court of examiners. The Hallett prize, given in connexion with the primary examination for the fellowship, was awarded to Russell Thomas Cumming Fraser. At the primary examination held recently in Dunedin 23 candidates were examined, of whom 13 were approved, and at the examination held in Madras 60 candidates were examined, of whom 21 were approved. It was decided to make no change in the subjects of the primary examination for the fellowship.

The following hospitals were approved, with the posts specified, for recognition for the six months' surgical practice required of candidates for the final fellowship examination :—

Royal Sussex Hospital, Brighton (3 house surgeons); Kent and Canterbury Hospital (2 house surgeons); Royal Surrey Hospital, Guildford (3 house surgeons); King George's Hospital, Ilford (resident surgical officer and 3 house surgeons); Queen Mary's Hospital for the East End (2 house surgeons); Royal South Hants and Southampton Hospital (3 house surgeons); Royal Hampshire Hospital, Winchester (resident surgical officer and 2 house surgeons); and York County Hospital (the senior house surgeon).

A message of greeting from the council is being carried by Sir Holburt Waring to the Royal Australasian College of Surgeons, whose new building he is opening in Melbourne on March 4th.

Mr. Cyril Howkins and Mr. Frank Coleman were re-elected to the dental section of the board of examiners in dental surgery. Dr. L. W. Proger, of the Bland-Sutton institute of pathology at the Middlesex Hospital, was appointed pathological curator of the museum. Mr. F. H. Bentley has been appointed by the Mackenzie-Mackinnon research fund committee to carry out for one year a research on the causation of keloids in the laboratories of the College. Mr. C. H. Fagge was appointed Hunterian orator for 1936; Prof. G. Grey Turner the Bradshaw lecturer for 1935; and Dr. Cecil Wall the next Thomas Vicary lecturer.

Mr. Victor Bonney was elected as the representative of the College on the Central Midwives Board for the year ending March 31st, 1936. Sir D'Arcy Power was nominated as the representative of the College on the council of the Queen's Institute of District Nursing for three years. Sir Holburt Waring was elected representative of the College on the medical advisory committee of the British Health Resorts Association.

A diploma of membership was granted to Michael Clarence Condillac. Diplomas were granted, jointly with the Royal College of Physicians, as follows :—

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*Psychological Medicine.*—Harriette G. Bogle, I. J. Davies, J. M. Edwards, M. V. Govindaswamy, Marion Greaves, T. E. Hurley, A. K. McCowan, G. S. Nightingale, G. B. Palmer, and J. C. Rohan.

*Laryngology and Otology.*—H. L. Anand, V. V. H. Hoakai, Dukhan Ram, and J. B. Whaley.

The council, having received a resolution passed at the last meeting of fellows and members, reaffirming that the members should have some representation on the council, adopted a reply stating that they were not prepared to reopen the question of altering the constitution of the college.

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The council of this society offers an honorarium of £25 for the best critical review dealing with any of the venereal diseases considered from any angle, the selected essay to become the property of the council, who will be at liberty to publish in the *British Journal of Venereal Diseases* any review offered in competition other than the one to which the prize is awarded. A competing review should contain about 6000 words, be typewritten on one side of the paper only, with a quarter of a page as a margin, and be sent to the hon. secretary, M.S.S.V.D., 43, Queen Anne-street, London, W. 1, before July 31st, 1935.

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President: Mr. L. E. C. Norbury; vice-presidents: Dr. Macdonald Critchley, Prof. Tom Hare, Dr. N. Gray Hill, Prof. C. A. Pannett; treasurer: Mr. C. P. G. Wakeley; secretaries: Dr. A. D. Morris and Mr. John Hunter; council: Dr. D. H. Brinton, Dr. F. S. Cooksey, Dr. A. Hope Gosse, Dr. Norman Hill, Dr. F. Hobday, Dr. T. C. Hunt, Dr. A. F. Morcom, Dr. A. D. Munro, Mr. W. E. Tanner, Dr. G. de Bec Turtle, Dr. R. R. Watts, and Mr. A. Dickson Wright.

## Salford Municipal Clinic

The times of the lectures and demonstrations in the course on venereal diseases which is being given at this clinic have been altered. They will now take place on Mondays and Thursdays at 3.30 P.M., and not as stated in our issue of Jan. 5th (p. 59).

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Five hundred pounds has been placed at the disposal of the scientific advisory committee for the year 1935 for the salary and expenses of a research worker to carry out, under supervision, an investigation of the action of radiation on colloids.

The affiliation of the National Cancer Association of South Africa to the British Empire Cancer Campaign was approved.

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The Jenner memorial medal of the Epidemiological Society (now merged in the Royal Society of Medicine as the section of epidemiology and State medicine) has been awarded, on the recommendation of the section, to Sir George Buchanan. He will receive the medal at the meeting of the section which is being held on Jan. 25th at 8.30 P.M. The medal was inaugurated in 1896 on the occasion of the Jenner centenary, and it is awarded for distinguished work in epidemiological research or for pre-eminence in the prevention and control of epidemic disease.

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This departure in publishing has been formed for the issue of authoritative technical books, and the first list of its forthcoming works will be found at the end of the spring list issued by Messrs. Hodder & Stoughton. English Universities Press, Ltd., is able to announce in this list volumes by, among others, Dr. H. Spencer Jones, the Astronomer Royal, who writes on the Wonders of the Heavens, and by Prof. H. Cotton, of University College, Nottingham, who writes on the Transmission and Distribution of Electrical Energy. Other treatises are announced from the hands of well-known authorities on such diverse subjects as aerodynamics, principles of architecture, use of electricity in rural industries, and gardening. The publications should therefore justify the general title adopted of "technical books," and Dr. F. H. Spencer, late chief inspector of education to the L.C.C., will be the general adviser in connexion with the series.

## Appointments

HAMBURGER, RICHARD, M.D. Rostock, L.R.C.P. Edin., has been appointed Hon. Assistant Physician to the Children's Department of the London Jewish Hospital.

HARPER, J. S., M.B. Aberd., D.P.H., County Tuberculosis Officer for Wiltshire.

Certifying Surgeons under the Factory and Workshop Acts: Dr. K. MCLAY (Galashiels, Selkirkshire); Dr. M. FOSTER (Herne Bay, Kent); Dr. N. R. HOUSTON (Tonbridge, Kent); and Dr. J. C. CAMERON (Muirkirk, Ayrshire).

## Vacancies

*For further information refer to the advertisement columns*

*Ashton-under-Lyne District Infirmary.*—H.S. At rate of £150.
*Belfast, Royal Victoria Hospital.*—Seven Res. H.S.'s.
*Birmingham, Children's Hospital.*—Asst. Res. M.O., &c. £125.
*Birmingham City.*—Asst. M.O. for Maternity and Child Welfare. £500.
*Birmingham and Midland Eye Hospital.*—Res. Surg. O. £200.
*Birmingham, Monyhull Colony.*—Res. Asst. M.O. £350.
*Bradford Royal Infirmary.*—H.P. and H.S. Each at rate of £135.
*British Post-Graduate Medical School, Hammersmith, W.*—Two First Assts. for Dept. of Surgery. £250–£500.
*City of London Hospital for Diseases of the Heart and Lungs, Victoria Park, E.*—H.P. At rate of £100.
*Constance-road Institution, East Dulwich, S.E.*—Asst. M.O. £250.
*Dulwich Hospital, East Dulwich-grove, S.E.*—Asst. M.O. £250.
*Eastbourne, Princess Alice Memorial Hospital.*—Res. H.S. £150.
*East Ham Memorial Hospital, Shrewsbury-road, E.*—Res. M.O. At rate of £200. H.P. At rate of £150.
*Edmonton, Urban District Council.*—M.O.H. £1000.
*Elizabeth Garrett Anderson Hospital, Euston-road, N.W.*—Med. Reg. £100. Also Asst. Radiologist. £100.
*Evelina Hospital for Sick Children, Southwark, S.E.*—H.P. At rate of £120.
*French Hospital and Dispensary, Shaftesbury-avenue, W.C.*—Jun. Res. M.O. £100.
*Greenwich, Dreadnought Hospital.*—Anæsthetist. 50 gns.
*Grimsby and District Hospital.*—Sen. and Jun. H.S.'s. £200 and £150 respectively.
*Harrow Urban District Council.*—Asst. M.O.H. £600.
*Hertford County Hospital.*—Sen. H.S. At rate of £200.
*Highgate Hospital, Dartmouth Park-hill, N.*—Asst. M.O. £250.
*Holborn and Finsbury Institution, Shepherdess-walk, N.*—Asst. M.O. £250.
*Hospital for Consumption and Diseases of Chest, Brompton.*—Asst. Director of Radiological Dept.
*Hospital of St. John and St. Elizabeth, 60, Grove End-road, N.W.*—Res. H.P. At rate of £100.
*Hull Royal Infirmary.*—H.S. to Oph. and Ear, Nose, and Throat Depts. Also Cas. O. Each at rate of £150.
*Ilford, King George Hospital.*—H.P. and H.S. Each at rate of £100. Also Hon. Dermatologist.
*Isle of Ely County.*—Asst. County M.O.H. and Asst. School M.O. £500.
*Liverpool, Fazakerley Sanatorium.*—Res. Asst. M.O. £200.
*London County Council.*—Physicist. £750. Also Part-time School M.O.'s. 30s. per session.
*London Jewish Hospital, Stepney Green, E.*—Ear, Nose, and Throat Registrar. 20 gns.
*London Lock Hospital, 91, Dean-street, W.*—Surg. Reg. £100.
*Lowestoft, St. Luke's Hospital.*—£350.
*Lucknow University.*—Professor Obstetrics and Gynæcology. Rs. 900/- p.m.
*Manchester, Crumpsall Hospital.*—Asst. M.O.'s. Each at rate of £200.
*Newcastle-upon-Tyne Hospital for Sick Children.*—H.P. and H.S. Each at rate of £100.
*Paddington Hospital, Harrow-road, W.*—Sen. Asst. M.O. £500.
*Paddington Metropolitan Borough.*—Visiting M.O. 1½ gns. per session.
*Prison Medical Service.*—M.O. £510 13s.
*Queen's Hospital for Children, Hackney-road, E.*—Asst. Phys. Also Clin. Asst. for Ophth. Dept.
*Queen Charlotte's Maternity Hospital, Marylebone-road, N.W.*—Obstet. Surgeon to Out-patients.
*Redhill, Royal Earlswood Institution.*—Jun. Asst. M.O. At rate of £250.
*Rotherham Hospital.*—Sen. H.S. £200. Also H.P. £180.
*Royal Dental Hospital, Leicester-square, W.C.*—Hon. Anæsthetist. Also Hon. Asst. Anæsthetist.
*Royal Masonic Hospital, Ravenscourt Park, W.*—Res. M.O. £300.
*Royal National Orthopædic Hospital, Great Portland-street, W.*—Hon. Radiologist.
*Sidcup, Queen Mary's Hospital.*—Asst. M.O. £250.
*St. Benedict's Hospital, Church-lane, S.W.*—Asst. M.O. £250.
*St. John's Hospital for Diseases of the Skin, Leicester-square, W.C.*—Two Hon. Asst. Physicians.
*St. Pancras Dispensary, 39, Oakley-square, N.W.*—Hon. Physician.
*Stoke-on-Trent, North Staffordshire Royal Infirmary.*—H.S. At rate of £150.
*Salisbury General Infirmary.*—H.P. At rate of £125.
*Southampton Free Eye Hospital.*—H.S. £150.
*Taunton, Sandhil Park, Bishop's Lydeard.*—Med. Supt. £850.
*Walsall County Borough.*—Asst. M.O.H. £500.
*Ware Park County Sanatorium, Hertford.*—Asst. M.O. £300.
*Westmorland County Hospital, Kendal.*—H.S. At rate of £200.

The Chief Inspector of Factories announces a vacant appointment for a Certifying Factory Surgeon at Old Deer, Aberdeenshire.

## Births, Marriages, and Deaths

### BIRTHS

LANGDALE-SMITH.—On Jan. 5th, the wife of H. G. Langdale Smith, M.B. Birm., Stechford, Birmingham, of a son.

O'FLYNN.—On Jan. 10th, at R.N. Hospital, Haslar, the wife of Surg.-Commander J. A. O'Flynn, M.D. N.U.I., R.N., of a son.

ORR.—On Jan. 14th, the wife of J. W. Orr, M.D. Belf., 8, North Hill-court, Headingley, Leeds, of a daughter.

SAVIN.—On Jan. 10th, at 174, Sutherland-avenue, W.9, the wife of L. H. Savin, M.D., M.S., M.R.C.P., F.R.C.S., of a son.

### MARRIAGES

D'ABREU—THROCKMORTON.—On Jan. 8th, in London, Alphonsus d'Abreu, M.B. Birm., F.R.C.S. Eng., to Elizabeth, elder daughter of the late Lieut.-Colonel Throckmorton and of Lady Throckmorton.

WATERS—MURPHY.—On Jan. 10th, at Bombay, Captain Harry Silvester Waters, M.B. Camb., F.R.C.S. Eng., I.M.S., elder son of Sir Harry Waters, late chief medical officer to the East India Railway, to Mary Lilette, only daughter of Mr. Justice Murphy, I.C.S.

### DEATHS

AVELINE.—On Jan. 10th, at Buchanan Hospital, St. Leonards, Henry Talbot Sidney Aveline, M.D. Durh., of Cooden-drive, Bexhill-on-Sea, late of Cotford, Taunton.

EVELYN.—On Jan. 6th, at Clifton, York, William Arthur Evelyn, M.D. Camb.

HAMILTON.—On Jan. 10th, at Holland-road, W., Benjamin Frazier Hamilton, M.R.C.S. Eng., Lieut.-Colonel, late R.A.M.C., in his 80th year.

HARDY.—On Jan. 10th, in a nursing-home, Herbert William Hardy, M.R.C.S. Eng., D.P.H., L.D.S., of Cromwell-road, S.W., formerly of Wakefield, aged 62.

HYDE.—On Jan. 9th, at Baggy Point, Croyde, North Devon, Edwin Hyde, M.R.C.S., L.R.C.P. Lond., aged 63.

LIDDERDALE.—On Jan. 8th, at Christchurch-road, Folkestone, Francis John Lidderdale, M.D. Camb.

LOW.—On Jan. 6th, at Lambeth Hospital, Robert Bruce Low, M.R.C.S. Eng., of Highfield, Peterston-super-Ely, Glamorgan, aged 53.

MATTHEWS.—On Jan. 7th, at St. Mark's-road, North Kensington, Arthur Kenward Matthews, M.R.C.S. Eng., aged 68.

MITCHELL.—On Jan. 9th, at Southport, Henry McCormick Mitchell, M.B. Aberd., of Rodney-street, Liverpool, aged 64 years.

REDMOND.—On Jan. 10th, at Elm Park-gardens, Chelsea, S.W., John Johnstone Redmond, L.R.C.P. & S.I., in his 71st year.

SALISBURY.—On Jan. 7th, very suddenly, at Woodlands, Billing-road, Northampton, Walter Salisbury, M.S. Lond., F.R.C.S. Eng., M.C.O.G., consulting surgeon Northampton General Hospital, aged 46.

WYLIE.—On Jan. 12th, suddenly, in Scotland, Andrew Wylie, M.D. Glasg., of Queen Anne-street, W., and Ulster-place, Regent's Park, aged 65.

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# MEDICAL NEWS

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*Hospital for Consumption and Diseases of Chest, Brompton.*—Asst. Director of Radiological Dept.
*Hospital of St. John and St. Elizabeth, 60, Grove End-road, N.W.*—Res. H.P. At rate of £100.
*Hull Royal Infirmary.*—H.S. to Oph. and Ear, Nose, and Throat Depts. Also Cas. O. Each at rate of £150.
*Ilford, King George Hospital.*—H.P. and H.S. Each at rate of £100. Also Hon. Dermatologist.
*Isle of Ely County.*—Asst. County M.O.H. and Asst. School M.O. £500.
*Liverpool, Fazakerley Sanatorium.*—Res. Asst. M.O. £200.
*London County Council.*—Physicist. £750. Also Part-time School M.O.'s. 30s. per session.
*London Jewish Hospital, Stepney Green, E.*—Ear, Nose, and Throat Registrar. 20 gns.
*London Lock Hospital, 91, Dean-street, W.*—Surg. Reg. £100.
*Lowestoft, St. Luke's Hospital.*—£350.
*Lucknow University.*—Professor Obstetrics and Gynæcology. Rs. 900/- p.m.
*Manchester, Crumpsall Hospital.*—Asst. M.O.'s. Each at rate of £200.
*Newcastle-upon-Tyne Hospital for Sick Children.*—H.P. and H.S. Each at rate of £100.
*Paddington Hospital, Harrow-road, W.*—Sen. Asst. M.O. £500.
*Paddington Metropolitan Borough.*—Visiting M.O. 1½ gns. per session.
*Prison Medical Service.*—M.O. £510 13s.
*Queen's Hospital for Children, Hackney-road, E.*—Asst. Phys. Also Clin. Asst. for Ophth. Dept.
*Queen Charlotte's Maternity Hospital, Marylebone-road, N.W.*—Obstet. Surgeon to Out-patients.
*Redhill, Royal Earlswood Institution.*—Jun. Asst. M.O. At rate of £250.
*Rotherham Hospital.*—Sen. H.S. £200. Also H.P. £180.
*Royal Dental Hospital, Leicester-square, W.C.*—Hon. Anæsthetist. Also Hon. Asst. Anæsthetist.
*Royal Masonic Hospital, Ravenscourt Park, W.*—Res. M.O. £300.
*Royal National Orthopædic Hospital, Great Portland-street, W.*—Hon. Radiologist.
*Sidcup, Queen Mary's Hospital.*—Asst. M.O. £250.
*St. Benedict's Hospital, Church-lane, S.W.*—Asst. M.O. £250.
*St. John's Hospital for Diseases of the Skin, Leicester-square, W.C.*—Two Hon. Asst. Physicians.
*St. Pancras Dispensary, 39, Oakley-square, N.W.*—Hon. Physician.
*Stoke-on-Trent, North Staffordshire Royal Infirmary.*—H.S. At rate of £150.
*Salisbury General Infirmary.*—H.P. At rate of £125.
*Southampton Free Eye Hospital.*—H.S. £150.
*Taunton, Sandhil Park, Bishop's Lydeard.*—Med. Supt. £850.
*Walsall County Borough.*—Asst. M.O.H. £500.
*Ware Park County Sanatorium, Hertford.*—Asst. M.O. £300.
*Westmorland County Hospital, Kendal.*—H.S. At rate of £200.

The Chief Inspector of Factories announces a vacant appointment for a Certifying Factory Surgeon at Old Deer, Aberdeenshire.

## Births, Marriages, and Deaths

### BIRTHS

LANGDALE-SMITH.—On Jan. 5th, the wife of H. G. Langdale Smith, M.B. Birm., Stechford, Birmingham, of a son.

O'FLYNN.—On Jan. 10th, at R.N. Hospital, Haslar, the wife of Surg.-Commander J. A. O'Flynn, M.D. N.U.I., R.N., of a son.

ORR.—On Jan. 14th, the wife of J. W. Orr, M.D. Belf., 8, North Hill-court, Headingley, Leeds, of a daughter.

SAVIN.—On Jan. 10th, at 174, Sutherland-avenue, W.9, the wife of L. H. Savin, M.D., M.S., M.R.C.P., F.R.C.S., of a son.

### MARRIAGES

D'ABREU—THROCKMORTON.—On Jan. 8th, in London, Alphonsus d'Abreu, M.B. Birm., F.R.C.S. Eng., to Elizabeth, elder daughter of the late Lieut.-Colonel Throckmorton and of Lady Throckmorton.

WATERS—MURPHY.—On Jan. 10th, at Bombay, Captain Harry Silvester Waters, M.B. Camb., F.R.C.S. Eng., I.M.S., elder son of Sir Harry Waters, late chief medical officer to the East India Railway, to Mary Lilette, only daughter of Mr. Justice Murphy, I.C.S.

### DEATHS

AVELINE.—On Jan. 10th, at Buchanan Hospital, St. Leonards, Henry Talbot Sidney Aveline, M.D. Durh., of Cooden-drive, Bexhill-on-Sea, late of Cotford, Taunton.

EVELYN.—On Jan. 6th, at Clifton, York, William Arthur Evelyn, M.D. Camb.

HAMILTON.—On Jan. 10th, at Holland-road, W., Benjamin Frazier Hamilton, M.R.C.S. Eng., Lieut.-Colonel, late R.A.M.C., in his 80th year.

HARDY.—On Jan. 10th, in a nursing-home, Herbert William Hardy, M.R.C.S. Eng., D.P.H., L.D.S., of Cromwell-road, S.W., formerly of Wakefield, aged 62.

HYDE.—On Jan. 9th, at Baggy Point, Croyde, North Devon, Edwin Hyde, M.R.C.S., L.R.C.P. Lond., aged 63.

LIDDERDALE.—On Jan. 8th, at Christchurch-road, Folkestone, Francis John Lidderdale, M.D. Camb.

LOW.—On Jan. 6th, at Lambeth Hospital, Robert Bruce Low, M.R.C.S. Eng., of Highfield, Peterston-super-Ely, Glamorgan, aged 53.

MATTHEWS.—On Jan. 7th, at St. Mark's-road, North Kensington, Arthur Kenward Matthews, M.R.C.S. Eng., aged 68.

MITCHELL.—On Jan. 9th, at Southport, Henry McCormick Mitchell, M.B. Aberd., of Rodney-street, Liverpool, aged 64 years.

REDMOND.—On Jan. 10th, at Elm Park-gardens, Chelsea, S.W., John Johnstone Redmond, L.R.C.P. & S.I., in his 71st year.

SALISBURY.—On Jan. 7th, very suddenly, at Woodlands, Billing-road, Northampton, Walter Salisbury, M.S. Lond., F.R.C.S. Eng., M.C.O.G., consulting surgeon Northampton General Hospital, aged 46.

WYLIE.—On Jan. 12th, suddenly, in Scotland, Andrew Wylie, M.D. Glasg., of Queen Anne-street, W., and Ulster-place, Regent's Park, aged 65.

*N.B.—A fee of 7s. 6d. is charged for the insertion of Notices of Births, Marriages, and Deaths.*

# NOTES, COMMENTS, AND ABSTRACTS

## PADUA AND ITS ENGLISH SCHOLARS*

By Dr. ARTURO CASTIGLIONI
PROFESSOR OF THE HISTORY OF MEDICINE, UNIVERSITY OF PADUA

IN the time in which a great passion for studies, a great love of beauty, and an inexhaustible desire for glory vivified all the works of the Italians, to Padua as the most important centre of scientific researches came students and teachers from all parts of Europe. Here the astronomers search the secret of the stars, the physicians the mystery of life, the mathematicians the most advanced problems of geometry and of algebra; from Copernicus to Galileo, from Vesalius to Fabrizio d'Acquapendente, from Colombo to Fracastoro, physicians, politicians, lawyers, physicists, naturalists, and mathematicians prepare and accomplish the Renaissance of Science. In Padua the great international currents meet; the far-seeing protection of a wise government preserves the freedom of teaching and of learning as a great treasure.

### ENGLISH STUDENTS AT PADUA

How important a part foreign students had in the life of the university, and particularly in the school of medicine, is demonstrated by the official records of the foreign nations in which are noted the most important happenings. And the keenness of the students is shown by the fact that sometimes their representatives would complain before the authorities because the lectures were not regularly delivered. In the year 1587 a few national groups were represented in the Natio Alemanna, that is the students from Switzerland, Bohemia, Denmark, Flanders, and Poland, and each group chose its representative. The English students were so numerous that in 1534 the Natio Anglica divided itself from the Scota; in 1603 the English, the Scotch, and the Irish are again united in the nation anglice. This nation had its own councillor, a beadle, and a secretary (*cancellarius*); it possessed also its own library and special privileges.

At the close of the XIVth century Duke Humphrey, of Gloucester, the youngest brother of that prototype of a medieval hero, Henry V., may be considered the patron of the revival of learning in England. He protected scholars such as Pecock, Capgrave, and Lydgate, the poet monk of Bury St. Edmund's, and brought over from Italy some of the younger humanists to instruct him in the ancient poets and orators. It was not, however, until later, towards the middle of the XVth century, that there was a continuous if slight stream of students from England to the Italian universities. Bologna had an English "natio" (or guild of students); Vicenza and Vercelli had English rectors, and many illustrious names appear on the register of Padua. The beginnings were small. A band of students, all Oxonians and most of them churchmen, set out separately in the middle of the XVth century for Italy. Tiptoft, Earl of Worcester, perhaps the original of the Italianate Englishman, accompanied them; he was not from Oxford and was afterwards to win a name for culture and cruelty. Of these students one, John Free of Bristol, studied medicine at Padua and afterwards taught it in different Italian cities. But modern English scholarship really begins with Grocyn, Linacre, and Latimer.

From the point of view of the historian of medicine Linacre is the most interesting of the three, though it was not medical studies that attracted him to Italy. He came in 1488 to study the humanities under the great Politian, who more than any in his day united profound erudition with innate grace of style. Linacre journeyed to Italy in the suite of his master and uncle William Selling, a Benedictine monk, who had been sent by Henry VII. on an embassy to the Pope; but he remained at Bologna to study under Politian, and later followed his teacher to Florence. There, it is interesting to note, he was admitted to attend the private instruction which Politian imparted to the young princes, Piero and Giovanni Medici, and it was to Giovanni, when he afterwards became Pope Leo X., that Linacre dedicated his edition of Galen in memory of their studies together. During his sojourn in Italy, Linacre won the esteem of some of the most notable men of his time, such as Aldus, the great Venetian printer, and Hermolaus Barbarus, the renowned Hellenist, and the latter urged him to translate Aristotle into Latin. It may have been the study of Aristotle that directed Linacre's attention towards natural science and medicine, for a few years later he graduated as a doctor of medicine at Padau. At Vicenza he pursued his medical studies under Leonicenus, who by advocating a return to the Hippocratic method had brought medical science back to the same sources from which the New Learning drew its strength. On his return to England, Linacre was not only an eminent humanist and the foremost physician of his time, but was the first Englishman who might claim to be considered *homo universalis*, a man of all-embracing culture, like his great Italian compeers. He lectured at Oxford, where he had More, Colet, and Erasmus as his pupils, and was appointed tutor to Henry VII.'s eldest son, Prince Arthur. At Oxford he lectured also in medicine, and Erasmus has considered him the introducer of medical science into England. Such was his distinction in medical practice in London that later he was chosen to be the successor of Battista de Boerio as King's physician, together with other doctors, among them John Chambers, who had also taken his degree at Padua. Linacre left his large fortune for the purpose of founding at Oxford and Cambridge chairs in medicine, and established the Royal College of Physicians of London on the model of similar Italian institutions. He was a shining example of wide culture, upright life, and public spirit. To his memory his countrymen owe a large debt of gratitude.

### CAIUS AND HARVEY

The work of Free and Linacre was continued in particular by Thomas Starkey, a student of Magdalen College, who took his degree at Padua and on his return from Italy became lecturer in medicine at Oxford. At Cambridge, too, the influence of the Paduan school of medicine was felt. The celebrated Dr. Caius had also studied at Padua, and the college at Cambridge, which still bears his name, in association with that of an older foundation, was richly endowed by him. Its original by-laws encouraged students to travel abroad to frequent the far-famed school of Padua, Bologna, Montpellier, or Paris. Caius did very much to advance the study of anatomy in England, and his college enjoyed the curious privilege, granted by the thrifty authorities of that time, of claiming annually the bodies of two executed criminals for the purpose of dissection.

A scholar of Gonville and Caius and the most illustrious of English students at Padua was William Harvey, whose immortal work is so well known that it would be superfluous to dwell on it. He matriculated at Padua in 1598 and his diploma, which is preserved at the College of Physicians, bears the date of April 25th, 1602. The degree was conferred on him by the Count Sigmund Capodilista with the usual ceremonies, that is by the books, the ring, the cap, and the kiss of peace. This custom was introduced in Oxford where it lasted at least till the middle of the XVIIth century, for it is described by Evelyn in his Diary. The custom to confer the medical degree with great solemnity in church, in the presence of the bishop and the authorities, was

* Abstract of an address delivered before the Royal Society of Medicine on Nov. 8th, 1934.

accepted widely till the Reformation. In 1574 Pius IV. (Giovanni Angelo dei Medici) issued a Bull "In Sacrosancta" requiring an oath of profession of the Catholic faith from those taking a degree. Non-Catholics, among them William Harvey, received their degrees from the Counts Palatine.

### THE COLLEGIO VENETO

In the face of the difficulties and disabilities involved in such a system the Republic of Venice by decree in 1616 instituted for non-Catholics the Collegio Veneto Artista, in which degrees were conferred by the authority of the College of Physicians; and when the Vatican protested vehemently the Republic answered through her councillor, "Fra Paolo" Sarpi, a scientist of renown, that it was not thought necessary that an excellent physician should be profound in theology. The Government of the Republic of Venice always defended with the greatest energy the rights of the foreign students of the University of Padua, who could freely send embassies to the Doge. The foundation of the Collegio Veneto was in itself a significant act, showing independence of spirit and political wisdom. From every part of the world, but especially from Poland, from Germany, and from France students came to Padua.

In the XVIIth century 127 English students obtained the degree in medicine by authority of the Collegio Veneto: among them some well-known scholars who became famous physicians in England.* But a greater number of English scholars stayed at Padua only one or two years, after having obtained previously their degrees in England; therefore their names are not in the list of the College. One of the most renowned of these students was John Evelyn, the great diarist and author of "Sylva," one of the promoters of the Royal Society; he was appointed by Charles II. to the original council of the society, and presented in 1650 to the society "a table of nerves and veines" prepared at Padua. Evelyn lived for a time in Padua in great style, occupying a handsome palace at the Piazza del Santo, the Cathedral Square of Padua, where many English students used to meet; among them were Henry Howard who was later Duke of Norfolk, Thomas Earl of Arundel, and Henry Brampton, a son of the Lord Keeper of the Seal of England.

With somewhat diminished glory the tradition is continued by Sir Richard Blackmore, whose highly moral ethic "Prince Arthur," though admired by Addison, so much amused the wits of his day. He graduated in medicine at Padua about the year 1680. More successful as a doctor than as a poet or a satirist or a versifier of Locke's philosophy, he was knighted in 1697 and appointed physician in ordinary to William III. and later to Anne. Thus it seems not to be an exaggeration when a chronicler of this time writes that there was no English noble family but displayed its coats-of-arms in the entrance court of the university of Padua.

When in 1688 the privilege to set up the coats-of-arms on the wall was abolished by the Senate of Venice, it was an English student, Richard Collins, Rector of the Faculty of Arts, to protest and to reclaim for his fellow students the right to inscribe their name. The old Paduan University had now assumed with great dignity a high cultural and political function. The hall of an old inn called *Il Bo'*, a name signifying "at the Sign of the Bull," and current among the university students to this day, was transformed into the magnificent historical hall in which thousands of inscriptions and of coats-of-arms tell the story of masters and students. These form documents or visual evidence of the great international current which flowed to Padua after the Renaissance from all the important centres of culture in the world. At the Padua of the Renaissance, the university where anatomical and physiological teaching had the most important success, there began experimental science.

* Prof. E. Morpurgo: English Physicians Doctorati at the University of Padua in the "Collegio Veneto Artista" (1617–1771). Proceedings of the Royal Society of Medicine, 1927, vol. xx., pp. 63–74.

## INJURIES IN SPORT

THE January issue of the *British Journal of Physical Medicine* contains a symposium in which the views upon injuries that occur in connexion with sport are set out by people qualified to speak on their subjects. Dr. Cove-Smith writes on the young male athlete and gives much advice as to the necessity of moderation, adding the wise sentiment that a knowledge of the nutritional and physical needs of the pre-adolescent would improve physical standards, and that those important people, the sports masters, should understand that excessive strains may interfere with growth. Dame Louise McIlroy, writing on the young woman athlete, concludes that open-air games and exercise are valuable in keeping the subjects fit, but may result in overstrain with serious after effects if engaged in at a time when the reproductive and endocrine functional changes are being adjusted. She considers it proved that there is very little disturbance of the menstrual function in the average girl who engages in games, daily exercise being often of value, and she alludes to inquiries on the subject made by herself in collaboration with Dr. Dundee among several thousand factory workers. The result, we are informed, was to show that dysmenorrhœa was rarely present among those of the women who did manual labour, though it was not infrequent among the clerks and typists. Other chapters are one on the treatment of paralysis due to spinal injury (Lieut.-Colonel E. L. Gowlland, M.B.), one on rider's strain (Sir Morton Smart, M.D.), one on the driving posture of the motorist (Dr. M. E. Ormsby), and one on the employment of infra-red and ultra-violet radiation in sprains (Dr. Annandale Troup). An essay on manipulative surgery in relation to athletic injuries (Mr. W. Eldon Tucker, F.R.C.S. Eng.) goes over ground that at the present moment is being much discussed, and here the value of manipulative measures and the contra-indications for their use are clearly set out. But has not the time arrived when something more definite should be said about slight subluxations, described as "a slight displacement of joint surfaces"? Mr. Tucker alludes to the scepticism which is manifested by medical men with regard to this condition, but supplies nothing to remove it. The presence of such displacements as those to which he alludes is not doubted by anyone; it is those invisible displacements seen by osteopaths, and said to be removable by osteopathy, concerning which incredulity is expressed; and their actuality and the procedure for their removal are regarded by osteopaths as the foundation of a system of general therapeutics.

## "IN THE DICTIONARY"

*To the Editor of* THE LANCET

SIR,—Are you aware that THE LANCET has arrived at the stage when it is included in a dictionary of ordinary language? I see that in the German-English Dictionary, by Karl Breul, M.A., Litt.D. (Cambridge), Ph.D. (Berlin), Schröder Professor of German in the University of Cambridge (published by Cassell) the English word "Lancet" is defined as "die Lanzette; Name einer medizinischen Zeitschrift." I am, Sir, yours faithfully,

Jan. 9th. BLANCUS.

*** Prosit Prof. Breul.—ED. L.

## FIRST-AID FOR GASSING

THE British Red Cross Society have issued a revised edition of this excellent little manual,[1] which was first published in 1929. Of the several booklets recently issued on the subject of gas warfare this is the most highly to be recommended; it has no point of view nor axe to grind. Written for the intelligent Red Cross worker it is yet well worth the attention of the medical profession, since it gives clearly and practically the essential first-aid treat-

[1] First Aid in Defence Against Chemical Warfare. By Major-General J. T. Collins, M.D., and Major H. S. Blackmore, M.R.C.S. London: Cassell and Co. Pp. 68. 6*d*.

ment of gas casualties—and it is immediate treatment which is all important. The usual classification is adopted and the points stressed in the treatment of the two most important groups, lung irritants and vesicants, are absolute rest, warmth, and oxygen in the case of the former and immediate removal of contamination with the use of watery, not oily, dressings in the case of the latter. Chapters are added on defensive measures and on gas-mask exercises, with care of the respirator. The two pages on gases which may be met with in civil life are too condensed to be of much value.

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STAGECRAFT.—Our advertisement columns contain particulars of a further course in dramatic production to be held at the Everyman Theatre, Hampstead, London, N.W. The attention of our readers is directed to this course because it is likely to help any who have to organise entertainments in hospitals or other institutions. It also provides instruction in the principles and practice of writing plays. The inaugural meeting will be held at the Everyman Theatre at 2.30 P.M. on Sunday, Feb. 10th.

VINETHENE: CORRIGENDUM.—In Sir Francis Shipway's paper in our last issue the statement is made (p. 83) that vinethene "possesses the best characteristics of ethylene chloride and of ether." This should read: "possesses the best characteristics of ethylene and of ether"; and we regret the error.

# Medical Diary

***Information to be included in this column should reach us in proper form on Tuesday, and cannot appear if it reaches us later than the first post on Wednesday morning.***

## SOCIETIES

ROYAL SOCIETY OF MEDICINE, 1, Wimpole-street, W.
TUESDAY, Jan. 22nd.
*Medicine.* 5 P.M. Dr. T. Izod Bennett: The Diagnosis of Diseases of the Stomach. Other speakers: Dr. Maurice Shaw and Dr. M. A. Arafa (Cairo) who will demonstrate his film of Gastroscopy.
WEDNESDAY.
*Comparative Medicine.* 5 P.M. Prof. J. Barcroft, Prof. F. C. Minett, and Dr. N. Hamilton Fairley: Hæmoglobinuria.
THURSDAY.
*Urology.* 8.30 P.M. Mr. Henry Wade and Mr. J. G. Yates Bell: The Treatment of Ureteric Calculi.
FRIDAY.
*Disease in Children.* 5 P.M. (Cases at 4.30 P.M.). Dr. T. S. Rodgers (for Dr. K. Tallerman): 1. Precocious Puberty. Dr. C. Allan Birch: 2. Subcutaneous Emphysema Complicating Pneumonia. Dr. K. D. Keele (for Dr. Bernard Schlesinger): 3. Cœliac Disease showing Unusual Features. Dr. A. M. Nussbrecher (by permission of Dr. A. Moncrieff): 4. Idiopathic Hypertrophy of Heart. 5. Amyotonia Congenita in a Boy aged 4½. Dr. R. W. B. Ellis: 6 and 7. X Ray and Post-mortem Specimens from (*a*) Lymphosarcoma involving the Heart: (*b*) Mediastinal Cyst. Dr. O. Richards: 8. Sclerema Neonatorum. 9. Case for Diagnosis. Dr. H. H. Chodak Gregory: 10. Lymphatic Leukæmia.
*Epidemiology and State Medicine.* 8.30 P.M. Dr. H. E. Magee: Assessment of the State of Nutrition.

BRITISH PSYCHOLOGICAL SOCIETY.
WEDNESDAY, Jan. 23rd.
*Medical Section.* 8.30 P.M. (1, Wimpole-street, W.), Dr. Emanuel Miller: The Present Discontent in Psychopathology.

ST. JOHN'S HOSPITAL DERMATOLOGICAL SOCIETY, 49, Leicester-square, W.C.
WEDNESDAY, Jan. 23rd.—5 P.M., Dr. R. R. Wettenhall: Practice of Dermatology in Melbourne, Australia.

MEDICO-LEGAL SOCIETY, 11, Chandos-street, W.
THURSDAY, Jan. 24th.—8.30 P.M., Dr. W. Norwood East: Murder from the point of view of the Psychiatrist.

SOCIETY OF MEDICAL OFFICERS OF HEALTH, 1, Upper Montague-street, W.C.
FRIDAY, Jan. 25th.
*Maternity and Child Welfare Group.*—8.30 P.M., Dr. Ian Suttie: Mental Factors in the Welfare of the Child.
*Dental Officers' Group.* 8 P.M., Mr. D. E Mason: Superannuation and Salaries.
*Fever Hospital Medical Service Group.* 4 P.M., Dr. J. M. Kennedy: Cerebro-spinal Meningitis.
SATURDAY.
*School Medical Service Group.* 2.45 P.M. (Elm Court Residential School for Blind Girls) Elm Court-road, S.E.), Meeting.

ROYAL SOCIETY OF ARTS, John-street, W.C.
WEDNESDAY, Jan. 23rd.—8 P.M., Mr. Charles L. Burdick: Humidity, Health, and Some New Inventions.

## LECTURES, ADDRESSES, DEMONSTRATIONS, &c.

ROYAL COLLEGE OF SURGEONS OF ENGLAND, Lincoln's Inn-fields, W.C. (Hunterian lectures.)
MONDAY, Jan. 21st.—5 P.M., Mr. T. Pomfret Kilner: Transplantation of the Skin.
WEDNESDAY.—5 P.M., Mr. Laurence O'Shaughnessy: Surgery of the Lung Root.
FRIDAY.—5 P.M., Dr. Macdonald Critchley: Morphology of the Cerebro-spinal Arteries and their Clinical Significance.

FELLOWSHIP OF MEDICINE AND POST-GRADUATE MEDICAL ASSOCIATION, 1, Wimpole-street, W.
MONDAY, Jan. 21st to SATURDAY, Jan. 26th.—NATIONAL HOSPITAL FOR DISEASES OF THE HEART, Westmoreland-street, W. All day course in cardiology. Open to all.—ST. PETER'S HOSPITAL, Henrietta-street, W.C. All day course in urology.—NATIONAL TEMPERANCE HOSPITAL, Hampstead-road, N.W. Tues., 8 P.M., Mr. R. C. Brock: Injuries to Bones. Thurs., 8 P.M., Mr. T. Holmes Sellors: Thorax.—WELLCOME MUSEUM OF MEDICAL SCIENCE, Euston-road, N.W. Thurs., 3 P.M., Dr. William Evans: Demonstration of Electrocardiograms.—MEDICAL SOCIETY OF LONDON, Chandos-street, W. Wed., 8.30 P.M., Dr. Kenneth Harris: Electrocardiograms (Interpretation of Tracings). Fri., 4.15 P.M. Dr. A. E. Clark-Kennedy: Vomiting.—Courses, clinics, &c., are open only to members and associates of the Fellowship.

HOSPITAL FOR SICK CHILDREN, Great Ormond-street, W.C.
MONDAY, Jan. 21st.—Noon, Dr. D. N. Nabarro: Congenital Syphilis: (1) General Consideration.
WEDNESDAY.—2 P.M., Dr. W. J. Pearson: Vomiting in Infancy.
THURSDAY.—Noon, Dr. A. G. Signy: Laboratory Tests for Congenital Syphilis.
FRIDAY.—Noon, Mr. L. E. Barrington-Ward: Congenital Abnormalities of the Intestine.
There will be out-patient clinics every day at 10 A.M. and Ward Visits (except on Wednesday) at 2 P.M.

WEST LONDON HOSPITAL POST-GRADUATE COLLEGE, Hammersmith, W.
MONDAY, Jan. 21st.—10 A.M., medical wards, skin clinic. 2 P.M., gynæcological and surgical wards, eye and gynæcological clinics. 4.15 P.M., Mr. Green-Armytage: Endocrine Dysfunction in Gynæcology and Obstetrics.
TUESDAY.—10 A.M., medical wards. 11 A.M., surgical wards. 2 P.M., throat clinic. 4.15 P.M., Dr. Konstam: Cardiac Arrhythmias.
WEDNESDAY.—10 A.M., childrens' ward and clinic. 2 P.M., medical wards, eye clinic. 4.15 P.M., Dr. Archer: Biochemical Demonstration.
THURSDAY.—10 A.M., neurological and gynæcological clinics. 11 A.M., fracture clinic. 2 P.M., eye and genito-urinary clinics.
FRIDAY.—10 A.M., skin clinic. Noon, lecture on treatment. 2 P.M., throat clinic. 4.15 P.M., Mr. Simpson-Smith: Abdominal Injuries.
SATURDAY.—10 A.M., medical wards, childrens' and surgical clinics.
The lectures at 4.15 P.M. are open to all medical practitioners without fee.

ROYAL INSTITUTION, 21, Albemarle-street, W.
THURSDAY, Jan. 24th.—5.15 P.M., Prof. H. Hartridge: Recent Advances in Vision and Hearing.

HOSPITAL FOR EPILEPSY AND PARALYSIS, Maida Vale, W.
THURSDAY, Jan. 24th.—3 P.M., Dr. Wilfred Harris: Demonstration.

LONDON SCHOOL OF DERMATOLOGY, 49, Leicester-square W.C.
TUESDAY, Jan. 22nd.—5 P.M., Dr. R. T. Brain: Psoriasis.
THURSDAY.—5 P.M., Dr. W. N. Goldsmith: Pigmentary Disorders. (Chesterfield lectures.)

CANCER HOSPITAL (FREE), Fulham-road, S.W.
THURSDAY, Jan. 24th.—4 P.M., Mr. Cecil Joll: Diagnosis and Treatment of Cancer of the Stomach.

CENTRAL LONDON THROAT, NOSE, AND EAR HOSPITAL, Gray's Inn-road, W.C.
FRIDAY, Jan. 25th.—4 P.M., Mr. A. Lowndes Yates: The Treatment of Deafness.

KING'S COLLEGE HOSPITAL MEDICAL SCHOOL, Denmark-hill, S.E.
THURSDAY, Jan. 24th.—9 P.M., Mr. H. L. C. Wood: Common Surgical Affections of the Rectum and Anus.

LEEDS GENERAL INFIRMARY.
TUESDAY, Jan. 22nd.—3.30 P.M., Mr. Black: Early Diagnosis of Glaucoma.

LEEDS PUBLIC DISPENSARY AND HOSPITAL.
WEDNESDAY, Jan. 23rd.—4 P.M., Dr. H. H. Moll: The Management of Pulmonary Tuberculosis.

NEWCASTLE GENERAL HOSPITAL.
SUNDAY, Jan. 20th.—10.30 A.M., Prof. T. Beattie: Medical Ward Visit.

GLASGOW POST-GRADUATE ASSOCIATION.
TUESDAY, Jan. 22nd.—3.30 P.M. (Faculty Hall, 242, St. Vincent-street), Dr. Ivy McKenzie: Some Unusual Forms of Cerebral Thrombosis.
WEDNESDAY.—4.15 P.M. (Royal Maternity and Women's Hospital), Prof. James Hendry: Obstetrical Cases.